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(54) **LIVER CANCER DETECTION KIT OR DEVICE, AND DETECTION METHOD**

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CPC C12Q 2600/158; C12Q 2600/178; C12Q 1/6886; C12Q 1/68; C12Q 1/6876
See application file for complete search history.

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(57) **ABSTRACT**

It is intended to provide a kit or device for the detection of liver cancer and a method for detecting liver cancer. The present invention relates to a kit or device for the detection of liver cancer, comprising a nucleic acid capable of specifically binding to miRNA in a sample of a subject, and a method for detecting liver cancer, comprising measuring the miRNA in vitro.

6 Claims, 4 Drawing Sheets

Specification includes a Sequence Listing.

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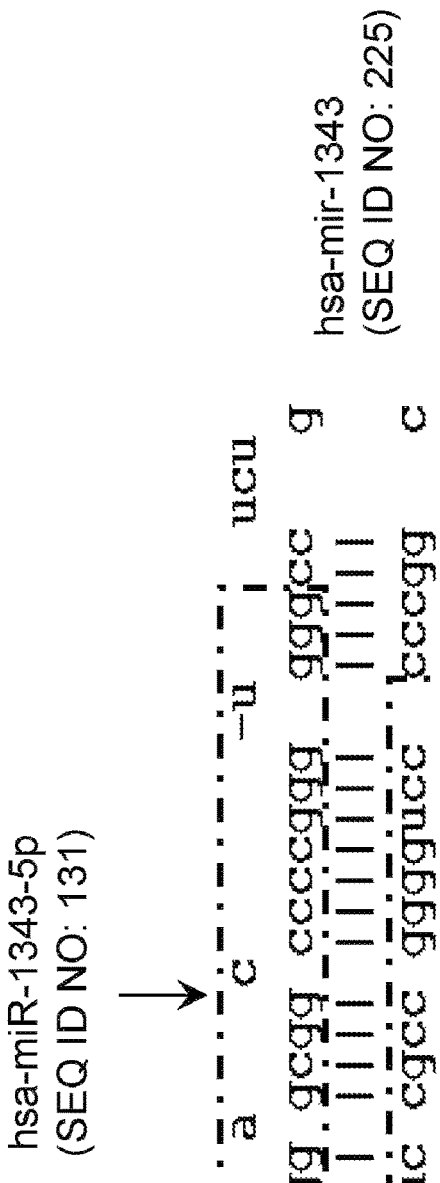
Fig. 1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(SEQ ID NO: 225)

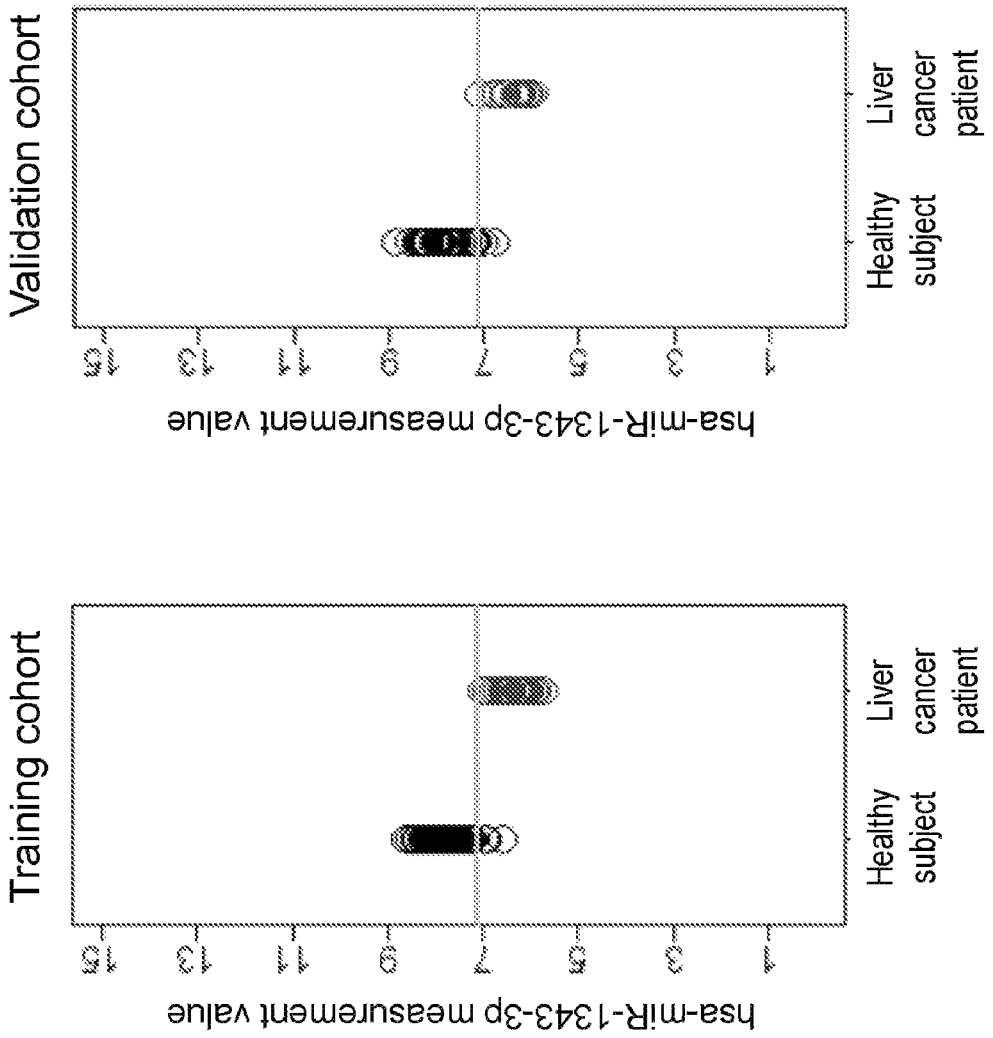
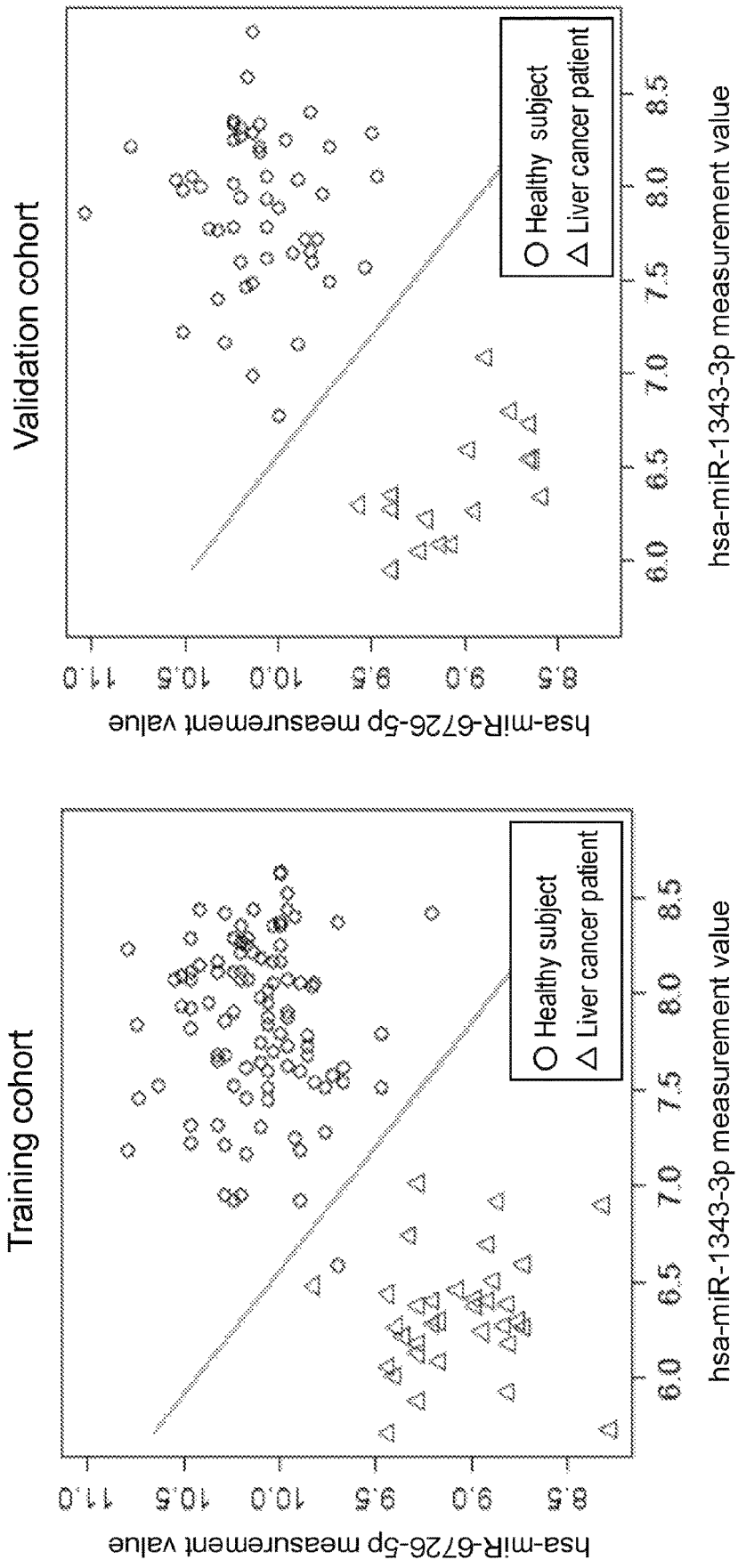

Validation cohort
hsa-miR-1343-3p measurement value
1
3
5
7
9
11
13
15
Healthy subject
Liver cancer patient
Training cohort
hsa-miR-1343-3p measurement value
1
3
5
7
9
11
13
15
Healthy subject
Liver cancer patient

Fig. 2

Fig. 3


Training cohort
Validation cohort
hsa-miR-6726-5p measurement value
hsa-miR-1343-3p measurement value
O Healthy subject
Δ Liver cancer patient
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9.0
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10.5
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6.0
6.5
7.0
7.5
8.0
8.5

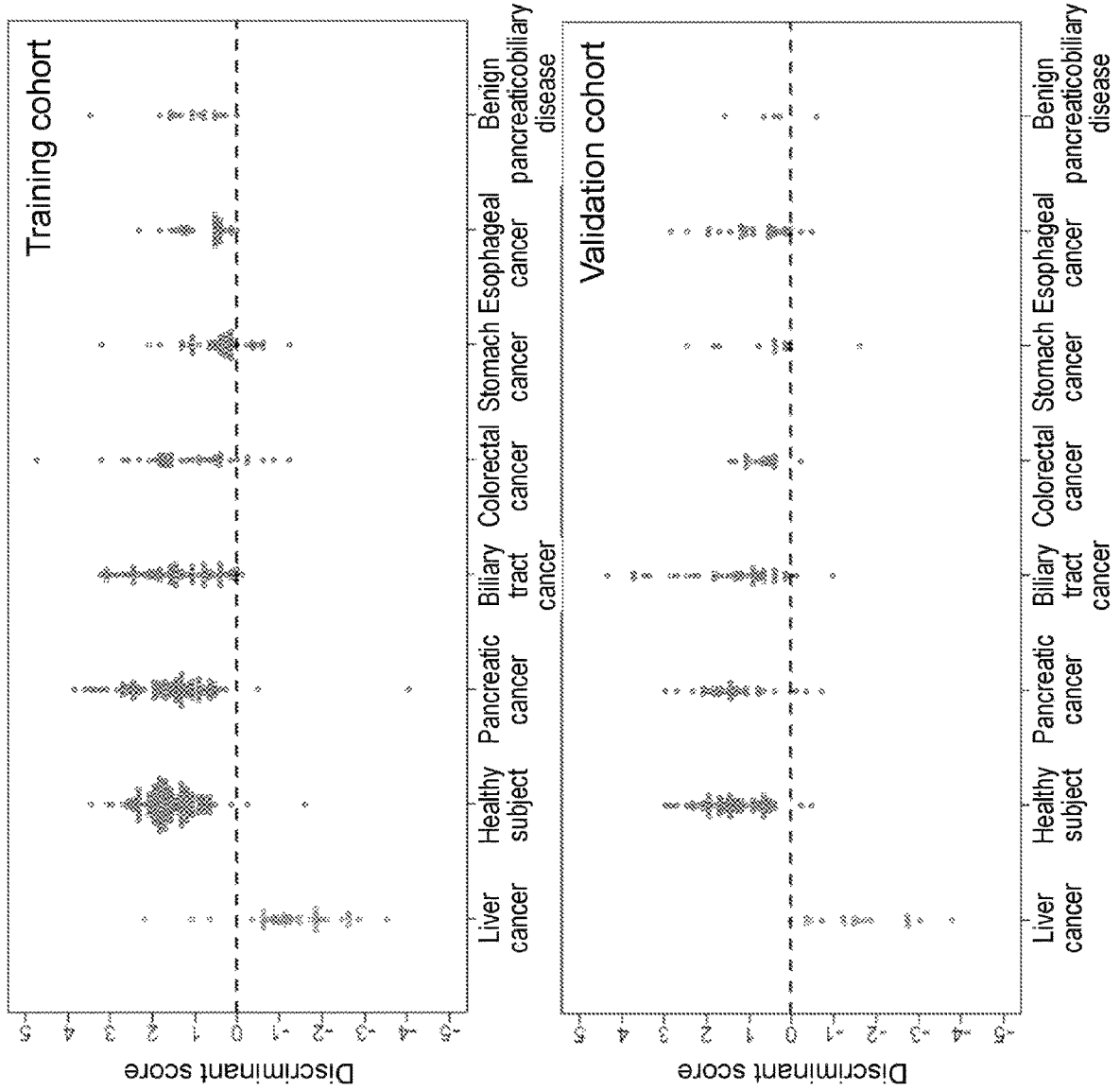
Training cohort
Validation cohort
Discriminant score
5
4
3
2
1
0
-1
-2
-3
-4
-5
Liver cancer
Healthy subject
Pancreatic cancer
Biliary tract cancer
Colorectal cancer
Stomach cancer
Esophageal cancer
Benign pancreaticobiliary disease

Fig. 4

LIVER CANCER DETECTION KIT OR DEVICE, AND DETECTION METHOD

TECHNICAL FIELD

The present invention relates to a kit or a device for the detection of liver cancer, comprising a nucleic acid capable of specifically binding to a particular miRNA, which is used for examining the presence or absence of liver cancer in a subject, and a method for detecting liver cancer, comprising measuring an expression level of the miRNA using the nucleic acid.

BACKGROUND ART

The liver is the largest organ in the body and is positioned in the upper right portion of the abdomen. Its main roles are the metabolism of nutrients and the detoxication and elimination of harmful substances. According to the 2011 statistics of cancer types in Japan disclosed by the Center for Cancer Control and Information Services, National Cancer Center, the number of individuals affected by liver cancer is 47,271 people. Namely, it is estimated that one out of every 35 Japanese individuals experience liver cancer. The number of individuals affected by liver cancer among other cancer types takes the 6th in place. Also, men are nearly twice as likely as women to develop liver cancer. The number of liver cancer deaths in men and women together climbed to 30,690 people and takes the 4th in place. An estimate of the number of American individuals affected by liver cancer in 2014 climbs to 33,190 people, among which approximately 23,000 people will die (Non-Patent Literature 1).

In general, primary liver cancer often refers to hepatocellular carcinoma which accounts for approximately 80% of primary liver cancer cases. However, there are other subtypes of primary liver cancer such as intrahepatic bile duct carcinoma which accounts for 10 to 20% of all primary liver cancer cases, and biliary cystadenocarcinoma which is a rarer cancer type.

The stages of liver cancer progression are specified separately for hepatocellular carcinoma and intrahepatic bile duct carcinoma in Non-Patent Literature 2. Herein, particularly, the hepatocellular carcinoma is classified into stage I (T1/N0/M0), stage II (T2/N0/M0), stage IIIA (T3a/NO/M0), stage IIIB (T3b/NO/M0), stage IIIC (T4/NO/M0), stage IVA (N1/M0), and stage IVB (M1) according to the degrees of tumor spread (T0 to T4), lymph node metastasis (N0 and N1), and distant metastasis (M0 and M1).

The 5-year relative survival rate of liver cancer differs depending on the stages of progression. According to Non-Patent Literature 1, the 5-year relative survival rate of liver cancer is reportedly 28% for tumors localized within liver (stage 1, stage 2 and some cases of stage 3), 7% for tumors found to have metastasized to a surrounding area of liver (stage IIIC and stage IVA), and 2% for tumors found to have metastasized distantly (stage IVB). Thus, the detection and treatment of liver cancer at an early stage before metastasis makes a significant contribution to improvement in the survival rate.

The treatment of liver cancer is performed mainly by 3 procedures: surgical therapy mainly involving resection and/or liver transplantation; local therapy which involves injecting a drug through centesis or performing cauterization to kill cancer; and hepatic arterial embolization. These procedures are used in combination with drug therapy or radiotherapy. Particularly, early liver cancer which is found not to metastasize to a blood vessel or an adjacent site is often cured by the partial resection of the liver (Non-Patent Literature 1). On the other hand, even if cancer is localized, liver transplantation is desirable for the cases where such resection is impossible on the ground that the tumors have a large size or are placed in proximity to a blood vessel, for example. If metastasis is found, systemic drug therapy or radiotherapy is performed (Non-Patent Literature 1).

As described in Non-Patent Literature 1, primary tests of liver cancer are inspection and palpation as well as imaging tests such as ultrasonography, CT scan, MRI scan, and angiography. For example, AFP (alpha fetoprotein) and PIVKA-II are known as tumor markers for the detection of liver cancer. The tests using these tumor markers are often performed in combination with ultrasonography. When there are findings that suspect liver cancer by these primary tests, pathological examination which involves inserting a needle into a lesion and collecting cells or tissues, which are then examined under a microscope is carried out as a secondary test.

Meanwhile, it is known that the most important leading cause of liver cancer is prolonged infection with hepatitis B or C virus. Therefore, subjects suspected of having liver cancer may be subjected to a hepatitis virus test in addition to the primary tests described above.

As shown in Patent Literatures 1 to 5, there are reports, albeit at a research stage, on methods for detecting liver cancer using the expression levels of microRNAs (miRNAs) in biological samples including blood and hepatic tissues.

Patent Literature 1 discloses a method for detecting leukemia, breast cancer, and liver cancer using miRNAs: hsa-miR-92a-3p, hsa-miR-92b-3p, hsa-miR-92a-2-5p, and hsa-miR-92b-5p in tissues as markers.

Patent Literature 2 has reported a method for diagnosing various cancers using, as markers, miRNAs such as hsa-miR-23a-3p, hsa-miR-23b-3p, hsa-miR-24-3p, hsa-miR-557, hsa-miR-564, hsa-miR-614, hsa-miR-150-3p, and hsa-miR-486-3p contained in vesicles circulating in body fluids.

Patent Literature 3 discloses a method for detecting various diseases including liver cancer using miRNAs such as hsa-miR-23b-3p, hsa-miR-30c-1-3p, hsa-miR-125a-3p, and hsa-miR-486-3p in tissues or body fluids as markers.

Patent Literature 4 discloses a method for detecting various pathological conditions including liver cancer using, as markers, miRNAs such as hsa-miR-16-5p, hsa-miR-92a-3p, hsa-miR-663a, hsa-miR-1913, and hsa-miR-625-3p, or proteins contained in vesicles circulating in body fluids.

Patent Literature 5 discloses that hsa-miR-187-5p, hsa-miR-92a-3p, hsa-miR-16-5p, and hsa-miR-30c-1-3p in plasma are markers for colorectal cancer, liver cancer, and lung cancer.

CITATION LIST

Patent Literature

Patent Literature 1: International Publication No. WO 2010/123043

Patent Literature 2: U.S. Patent Application Publication No. 2011/003704

Patent Literature 3: International Publication No. WO 2010/054386

Patent Literature 4: International Publication No. WO 2012/174282

Patent Literature 5: International Publication No. WO 2011/076142

Non-Patent Literature

Non-Patent Literature 1: American Cancer Society, "Liver Cancer", 2013, p. 5 to 8, 14 to 15, 17 to 23, and 27 to 41

Non-Patent Literature 2: Sobin, L. et al., "TNM Classification of Malignant Tumours, the 7th edition", 2010, p. 104-107

Non-Patent Literature 3: NCCN Guidelines, "Hepatobiliary Cancers, the 2nd edition", 2014, MS-4

Non-Patent Literature 4: Zhang, B and Yang, B., 1999, Journal of Medical Screening, Vol. 6 (2), p. 108-110

Non-Patent Literature 5: Takahashi, A. et al., 2008, World Journal of Gastroenterology, Vol. 14 (1), p. 129-31

SUMMARY OF INVENTION

Problem to be Solved by Invention

An object of the present invention is to find a novel tumor marker for liver cancer and to provide a method that can effectively detect liver cancer using a nucleic acid capable of specifically binding to the marker.

Liver cancer progresses without particular symptoms and is therefore difficult to detect early. Since the most part of the liver is housed in the right rib, liver cancer is difficult to detect by palpation. An effective method for liver cancer screening has not yet been established for ordinary people lacking a risk of liver cancer such as hepatitis virus infection or liver cirrhosis (Non-Patent Literature 1). Ultrasonography is a widely prevalent method for liver cancer screening because this method places less burden on patients and is convenient. Nonetheless, liver cancer may be difficult to detect depending on its site of occurrence by ultrasonography. In addition, examination results of ultrasonography largely depend on the skill of technicians. Therefore, it is considered to be desirable that ultrasonography should be used in combination with a tumor marker (Non-Patent Literature 3). Although AFP is known as a tumor marker for the detection of liver cancer, liver cancer found to have an elevated level of AFP is already at an advanced stage and is impossible to resect or has metastasized to an area outside the liver in many cases (Non-Patent Literature 1). It has been reported that some liver cancers do not produce AFP. Meanwhile, AFP is known to also elevate in cancers other than liver cancer, for example, testicular cancer or ovary cancer, and further to elevate in non-cancer liver diseases, for example, sustained hepatitis virus infection, and is therefore regarded as a low specific marker (Non-Patent Literature 1). For example, false diagnosis of other cancers as liver cancer wastes appropriate therapeutic opportunity or places unnecessary economical and physical burdens on patients due to the application of wrong medicine. According to results of large-scale screening research targeting hepatitis B-infected people and prolonged hepatitis patients (Non-Patent Literature 4), the AFP test has liver cancer detection sensitivity as low as 69% and thus has insufficient examination performance for use as a liver cancer screening test. Furthermore, CT scan or MRI scan can detect liver cancer with high performance, but is not suitable as a widely prevalent primary test because these tests require a specific apparatus and high examination cost.

As described below, there are reports, albeit at a research stage, on the determination of liver cancer using the expression levels of microRNAs (miRNAs) in biological samples including blood, none of which, however, have yet been brought into practical use.

Patent Literature 1 discloses a method for detecting leukemia, breast cancer, and liver cancer using miRNAs hsa-miR-92a-3p, hsa-miR-92b-3p, hsa-miR-92a-2-5p, and hsa-miR-92b-5p in blood cells or tissues as markers. This detection method, however, inevitably requires tissue resection by surgical operation for obtaining samples, and this step places a heavy physical burden on patients. Therefore, this method is not favorable as an examination method. In addition, Patent Literature 1 does not describe specific detection performance such as accuracy, sensitivity, or specificity for determining liver cancer as to this detection method, which is thus industrially less practical.

Patent Literature 2 has reported a method for diagnosing various cancers using, as markers, miRNAs such as hsa-miR-23a-3p, hsa-miR-23b-3p, hsa-miR-24-3p, hsa-miR-557, hsa-miR-564, hsa-miR-614, hsa-miR-150-3p, and hsa-miR-486-3p contained in vesicles circulating in body fluids. Patent Literature 2, however, neither describes a specific method for diagnosing liver cancer by use of this detection method nor describes detection performance such as accuracy, sensitivity, or specificity for determining liver cancer. Therefore, this detection method is industrially less practical.

Patent Literature 3 discloses a method for detecting various diseases including liver cancer using miRNAs such as hsa-miR-23b-3p, hsa-miR-30c-1-3p, hsa-miR-125a-3p, and hsa-miR-486-3p in tissues or body fluids as markers. This detection method, however, is based on results of experiments using mouse models, and the detection of liver cancer in humans is unknown about the method. In addition, Patent Literature 3 does not describe detection performance such as accuracy, sensitivity, or specificity for determining liver cancer. Therefore, this detection method is industrially less practical.

Patent Literature 4 discloses a method for detecting various pathological conditions including liver cancer using, as markers, miRNAs such as hsa-miR-16-5p, hsa-miR-92a-3p, hsa-miR-663a, hsa-miR-1913, and hsa-miR-625-3p, or proteins contained in vesicles circulating in body fluids. Patent Literature 4, however, neither describes a specific method for diagnosing liver cancer by use of this detection method nor validated these miRNA markers in an independent sample group. Therefore, this detection method is less reliable.

Patent Literature 5 discloses that hsa-miR-187-5p, hsa-miR-92a-3p, hsa-miR-16-5p, and hsa-miR-30c-1-3p in plasma are markers for colorectal cancer, liver cancer, and lung cancer. These markers, however, are markers for discriminating a group of colorectal cancers from a group of liver cancers, lung cancers, and healthy subjects and is not a marker for detecting liver cancer.

As mentioned above, the existing tumor markers exhibit low performance in the detection of liver cancer, and neither performance nor detection methods are specifically shown as to the markers at a research stage. Therefore, use of these markers might lead to carrying out needless extra examination due to the false detection of healthy subjects as being liver cancer patients, or might waste therapeutic opportunity because of overlooking liver cancer patients. In addition, the measurement of several dozens to several hundreds of miRNAs increases examination cost and is therefore difficult to use in large-scale screening such as medical checkup. Furthermore, the collection of liver tissues for measuring the tumor markers is highly invasive to patients and is not favorable. Hence, there is a demand for a highly accurate liver cancer marker that is detectable from blood, which can be collected with limited invasiveness, and is capable of correctly determining a liver cancer patient as a liver cancer patient and a healthy subject as a healthy subject. Particularly, the early detection and treatment of liver cancer can improve the survival rates. In addition, such liver cancer is often cured by the partial resection of the liver. Therefore, a

highly sensitive liver cancer marker capable of detecting liver cancer even at an early stage of progression is desired.

Means for Solution of Problem

The present inventors have conducted diligent studies to attain the object and consequently completed the present invention by finding multiple genes usable as markers for the detection of liver cancer from blood, which can be collected with limited invasiveness, and finding that liver cancer can be significantly detected by using nucleic acid(s) capable of specifically binding to any of these markers.

SUMMARY OF INVENTION

Specifically, the present invention has the following features:

(1) A kit for the detection of liver cancer, comprising nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of liver cancer markers: miR-1343-3p, miR-6726-5p, miR-6515-3p, miR-4651, miR-4257, miR-3188, miR-6131, miR-6766-3p, miR-7641, miR-1249, miR-3679-3p, miR-6787-5p, miR-4454, miR-3135b, miR-6765-3p, miR-7975, miR-204-3p, miR-7977, miR-7110-5p, miR-6717-5p, miR-6870-5p, miR-663b, miR-6875-5p, miR-8072, miR-6816-5p, miR-4281, miR-6729-5p, miR-8069, miR-4706, miR-7108-5p, miR-4433b-3p, miR-6893-5p, miR-6857-5p, miR-1227-5p, miR-6741-5p, miR-451a, miR-8063, miR-3622a-5p, miR-615-5p, miR-128-1-5p, miR-6825-5p, miR-1260b, miR-4433-3p, miR-4665-5p, miR-7845-5p, miR-1908-5p, miR-6840-3p, miR-6765-5p, miR-296-5p, miR-3675-3p, miR-6781-5p, miR-423-5p, miR-3663-3p, miR-6784-5p, miR-6749-5p, miR-1231, miR-4746-3p, miR-6780b-5p, miR-4758-5p, miR-3679-5p, miR-3184-5p, miR-6125, miR-6721-5p, miR-6791-5p, miR-3185, miR-1260a, miR-3197, miR-6845-5p, miR-6887-5p, miR-6738-5p, miR-6872-3p, miR-4497, miR-1229-5p, miR-6820-5p, miR-6777-5p, miR-3917, miR-5787, miR-4286, miR-6877-5p, miR-1225-3p, miR-6088, miR-6800-5p, miR-1246, miR-4467, miR-4419b, miR-1914-3p, miR-4632-5p, miR-1915-5p, miR-3940-5p, miR-1185-2-3p, miR-6746-5p, miR-5001-5p, miR-1228-5p, miR-5572, miR-4327, miR-4638-5p, miR-6799-5p, miR-6861-5p, miR-6727-5p, miR-4513, miR-6805-3p, miR-6808-5p, miR-4449, miR-1199-5p, miR-1275, miR-4792, miR-4443, miR-6891-5p, miR-6826-5p, miR-6807-5p, miR-7150, miR-4534, miR-4476, miR-4649-5p, miR-4525, miR-1915-3p, miR-4516, miR-4417, miR-642b-3p, miR-3141, miR-5100, miR-6848-5p, miR-4739, miR-4459, miR-1237-5p, miR-296-3p, miR-4665-3p, miR-6786-5p, miR-4258, miR-6510-5p, miR-1343-5p, miR-1247-3p, miR-6805-5p, miR-4492, miR-1469, miR-1268b, miR-6858-5p, miR-3937, miR-939-5p, miR-3656, miR-744-5p, miR-4687-3p, miR-4763-3p, miR-3620-5p, miR-3195, miR-6842-5p, miR-4707-5p, miR-642a-3p, miR-7113-3p, miR-4728-5p, miR-5195-3p, miR-1185-1-3p, miR-6774-5p, miR-8059, miR-3131, miR-7847-3p, miR-4463, miR-128-2-5p, miR-4508, miR-6806-5p, miR-7111-5p, miR-6782-5p, miR-4734, miR-3162-5p, miR-887-3p, miR-6752-5p, miR-6724-5p, miR-6757-5p, miR-4448, miR-671-5p, miR-3178, miR-4725-3p, miR-940, miR-6789-5p, miR-4484, miR-4634, miR-4745-5p, miR-4730, miR-6803-5p, miR-6798-5p, miR-3648, miR-4783-3p and miR-6836-3p.

(2) The kit according to (1), wherein miR-1343-3p is hsa-miR-1343-3p, miR-6726-5p is hsa-miR-6726-5p, miR-6515-3p is hsa-miR-6515-3p, miR-4651 is hsa-miR-4651, miR-4257 is hsa-miR-4257, miR-3188 is hsa-miR-3188, miR-6131 is hsa-miR-6131, miR-6766-3p is hsa-miR-6766-3p, miR-7641 is hsa-miR-7641, miR-1249 is hsa-miR-1249, miR-3679-3p is hsa-miR-3679-3p, miR-6787-5p is hsa-miR-6787-5p, miR-4454 is hsa-miR-4454, miR-3135b is hsa-miR-3135b, miR-6765-3p is hsa-miR-6765-3p, miR-7975 is hsa-miR-7975, miR-204-3p is hsa-miR-204-3p, miR-7977 is hsa-miR-7977, miR-7110-5p is hsa-miR-7110-5p, miR-6717-5p is hsa-miR-6717-5p, miR-6870-5p is hsa-miR-6870-5p, miR-663b is hsa-miR-663b, miR-6875-5p is hsa-miR-6875-5p, miR-8072 is hsa-miR-8072, miR-6816-5p is hsa-miR-6816-5p, miR-4281 is hsa-miR-4281, miR-6729-5p is hsa-miR-6729-5p, miR-8069 is hsa-miR-8069, miR-4706 is hsa-miR-4706, miR-7108-5p is hsa-miR-7108-5p, miR-4433b-3p is hsa-miR-4433b-3p, miR-6893-5p is hsa-miR-6893-5p, miR-6857-5p is hsa-miR-6857-5p, miR-1227-5p is hsa-miR-1227-5p, miR-6741-5p is hsa-miR-6741-5p, miR-451a is hsa-miR-451a, miR-8063 is hsa-miR-8063, miR-3622a-5p is hsa-miR-3622a-5p, miR-615-5p is hsa-miR-615-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-6825-5p is hsa-miR-6825-5p, miR-1260b is hsa-miR-1260b, miR-4433-3p is hsa-miR-4433-3p, miR-4665-5p is hsa-miR-4665-5p, miR-7845-5p is hsa-miR-7845-5p, miR-1908-5p is hsa-miR-1908-5p, miR-6840-3p is hsa-miR-6840-3p, miR-6765-5p is hsa-miR-6765-5p, miR-296-5p is hsa-miR-296-5p, miR-3675-3p is hsa-miR-3675-3p, miR-6781-5p is hsa-miR-6781-5p, miR-423-5p is hsa-miR-423-5p, miR-3663-3p is hsa-miR-3663-3p, miR-6784-5p is hsa-miR-6784-5p, miR-6749-5p is hsa-miR-6749-5p, miR-1231 is hsa-miR-1231, miR-4746-3p is hsa-miR-4746-3p, miR-6780b-5p is hsa-miR-6780b-5p, miR-4758-5p is hsa-miR-4758-5p, miR-3679-5p is hsa-miR-3679-5p, miR-3184-5p is hsa-miR-3184-5p, miR-6125 is hsa-miR-6125, miR-6721-5p is hsa-miR-6721-5p, miR-6791-5p is hsa-miR-6791-5p, miR-3185 is hsa-miR-3185, miR-1260a is hsa-miR-1260a, miR-3197 is hsa-miR-3197, miR-6845-5p is hsa-miR-6845-5p, miR-6887-5p is hsa-miR-6887-5p, miR-6738-5p is hsa-miR-6738-5p, miR-6872-3p is hsa-miR-6872-3p, miR-4497 is hsa-miR-4497, miR-1229-5p is hsa-miR-1229-5p, miR-6820-5p is hsa-miR-6820-5p, miR-6777-5p is hsa-miR-6777-5p, miR-3917 is hsa-miR-3917, miR-5787 is hsa-miR-5787, miR-4286 is hsa-miR-4286, miR-6877-5p is hsa-miR-6877-5p, miR-1225-3p is hsa-miR-1225-3p, miR-6088 is hsa-miR-6088, miR-6800-5p is hsa-miR-6800-5p, miR-1246 is hsa-miR-1246, miR-4467 is hsa-miR-4467, miR-4419b is hsa-miR-4419b, miR-1914-3p is hsa-miR-1914-3p, miR-4632-5p is hsa-miR-4632-5p, miR-1915-5p is hsa-miR-1915-5p, miR-3940-5p is hsa-miR-3940-5p, miR-1185-2-3p is hsa-miR-1185-2-3p, miR-6746-5p is hsa-miR-6746-5p, miR-5001-5p is hsa-miR-5001-5p, miR-1228-5p is hsa-miR-1228-5p, miR-5572 is hsa-miR-5572, miR-4327 is hsa-miR-4327, miR-4638-5p is hsa-miR-4638-5p, miR-6799-5p is hsa-miR-6799-5p, miR-6861-5p is hsa-miR-6861-5p, miR-6727-5p is hsa-miR-6727-5p, miR-4513 is hsa-miR-4513, miR-6805-3p is hsa-miR-6805-3p, miR-6808-5p is hsa-miR-6808-5p, miR-4449 is hsa-miR-4449, miR-1199-5p is hsa-miR-1199-5p, miR-1275 is hsa-miR-1275, miR-4792 is hsa-miR-4792, miR-4443 is hsa-miR-4443, miR-6891-5p is hsa-miR-6891-5p, miR-6826-5p is hsa-miR-6826-5p, miR-6807-5p is hsa-miR-6807-5p, miR-7150 is hsa-miR-7150, miR-4534 is hsa-miR-4534, miR-4476 is hsa-miR-4476, miR-4649-5p is hsa-miR-4649-5p, miR-4525 is hsa-miR-4525, miR-1915-3p is hsa-miR-1915-3p, miR-4516 is hsa-miR-4516, miR-4417 is hsa-miR-4417, miR-642b-3p is hsa-miR-642b-3p, miR-3141 is hsa-miR-3141, miR-5100 is hsa-miR-5100, miR-6848-5p is hsa-miR-6848-5p, miR-4739 is hsa-miR-4739, miR-4459 is hsa-miR-

4459, miR-1237-5p is hsa-miR-1237-5p, miR-296-3p is hsa-miR-296-3p, miR-4665-3p is hsa-miR-4665-3p, miR-6786-5p is hsa-miR-6786-5p, miR-4258 is hsa-miR-4258, miR-6510-5p is hsa-miR-6510-5p, miR-1343-5p is hsa-miR-1343-5p, miR-1247-3p is hsa-miR-1247-3p, miR-6805-5p is hsa-miR-6805-5p, miR-4492 is hsa-miR-4492, miR-1469 is hsa-miR-1469, miR-1268b is hsa-miR-1268b, miR-6858-5p is hsa-miR-6858-5p, miR-3937 is hsa-miR-3937, miR-939-5p is hsa-miR-939-5p, miR-3656 is hsa-miR-3656, miR-744-5p is hsa-miR-744-5p, miR-4687-3p is hsa-miR-4687-3p, miR-4763-3p is hsa-miR-4763-3p, miR-3620-5p is hsa-miR-3620-5p, miR-3195 is hsa-miR-3195, miR-6842-5p is hsa-miR-6842-5p, miR-4707-5p is hsa-miR-4707-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7113-3p is hsa-miR-7113-3p, miR-4728-5p is hsa-miR-4728-5p, miR-5195-3p is hsa-miR-5195-3p, miR-1185-1-3p is hsa-miR-1185-1-3p, miR-6774-5p is hsa-miR-6774-5p, miR-8059 is hsa-miR-8059, miR-3131 is hsa-miR-3131, miR-7847-3p is hsa-miR-7847-3p, miR-4463 is hsa-miR-4463, miR-128-2-5p is hsa-miR-128-2-5p, miR-4508 is hsa-miR-4508, miR-6806-5p is hsa-miR-6806-5p, miR-7111-5p is hsa-miR-7111-5p, miR-6782-5p is hsa-miR-6782-5p, miR-4734 is hsa-miR-4734, miR-3162-5p is hsa-miR-3162-5p, miR-887-3p is hsa-miR-887-3p, miR-6752-5p is hsa-miR-6752-5p, miR-6724-5p is hsa-miR-6724-5p, miR-6757-5p is hsa-miR-6757-5p, miR-4448 is hsa-miR-4448, miR-671-5p is hsa-miR-671-5p, miR-3178 is hsa-miR-3178, miR-4725-3p is hsa-miR-4725-3p, miR-940 is hsa-miR-940, miR-6789-5p is hsa-miR-6789-5p, miR-4484 is hsa-miR-4484, miR-4634 is hsa-miR-4634, miR-4745-5p is hsa-miR-4745-5p, miR-4730 is hsa-miR-4730, miR-6803-5p is hsa-miR-6803-5p, miR-6798-5p is hsa-miR-6798-5p, miR-3648 is hsa-miR-3648, miR-4783-3p is hsa-miR-4783-3p, and miR-6836-3p is hsa-miR-6836-3p.

(3) The kit according to (1) or (2), wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(b) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729,

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

(4) The kit according to any of (1) to (3), wherein the kit further comprises nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of other liver cancer markers: miR-23b-3p, miR-23a-3p, miR-625-3p, miR-1228-3p, miR-614, miR-1913, miR-92a-2-5p, miR-187-5p, miR-16-5p, miR-92b-3p, miR-150-3p, miR-564, miR-125a-3p, miR-92b-5p, miR-92a-3p and miR-663a.

(5) The kit according to (4), wherein miR-23b-3p is hsa-miR-23b-3p, miR-23a-3p is hsa-miR-23a-3p, miR-625-3p is hsa-miR-625-3p, miR-1228-3p is hsa-miR-1228-3p, miR-614 is hsa-miR-614, miR-1913 is hsa-miR-1913, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-187-5p is hsa-miR-187-5p, miR-16-5p is hsa-miR-16-5p, miR-92b-3p is hsa-miR-92b-3p, miR-150-3p is hsa-miR-150-3p, miR-564 is hsa-miR-564, miR-125a-3p is hsa-miR-125a-3p, miR-92b-5p is hsa-miR-92b-5p, miR-92a-3p is hsa-miR-92a-3p, and miR-663a is hsa-miR-663a.

(6) The kit according to (4) or (5), wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (f) to (j):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183,

(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides, (i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i).

(7) The kit according to any of (1) to (6), wherein the kit further comprises nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of other liver cancer markers: miR-4688, miR-4648, miR-6085, miR-6126, miR-6880-5p, miR-328-5p, miR-6768-5p, miR-3180, miR-6087, miR-1273g-3p, miR-1225-5p, miR-3196, miR-4695-5p, miR-6732-5p, miR-638, miR-6813-5p, miR-665, miR-486-3p, miR-4466, miR-30c-1-3p, miR-3621, miR-6743-5p, miR-4298, miR-4741, miR-3619-3p, miR-6824-5p, miR-5698, miR-371a-5p, miR-4488, miR-1233-5p, miR-4723-5p, miR-24-3p, miR-1238-5p, miR-4442, miR-3928-3p, miR-6716-5p, miR-6089, miR-6124, miR-6778-5p, miR-557 and miR-6090.

(8) The kit according to (7), wherein miR-4688 is hsa-miR-4688, miR-4648 is hsa-miR-4648, miR-6085 is hsa-miR-6085, miR-6126 is hsa-miR-6126, miR-6880-5p is hsa-miR-6880-5p, miR-328-5p is hsa-miR-328-5p, miR-6768-5p is hsa-miR-6768-5p, miR-3180 is hsa-miR-3180, miR-6087 is hsa-miR-6087, miR-1273g-3p is hsa-miR-1273g-3p, miR-1225-5p is hsa-miR-1225-5p, miR-3196 is hsa-miR-3196, miR-4695-5p is hsa-miR-4695-5p, miR-6732-5p is hsa-miR-6732-5p, miR-638 is hsa-miR-638, miR-6813-5p is hsa-miR-6813-5p, miR-665 is hsa-miR-665, miR-486-3p is hsa-miR-486-3p, miR-4466 is hsa-miR-4466, miR-30c-1-3p is hsa-miR-30c-1-3p, miR-3621 is hsa-miR-3621, miR-6743-5p is hsa-miR-6743-5p, miR-4298 is hsa-miR-4298, miR-4741 is hsa-miR-4741, miR-3619-3p is hsa-miR-3619-3p, miR-6824-5p is hsa-miR-6824-5p, miR-5698 is hsa-miR-5698, miR-371a-5p is hsa-miR-371a-5p, miR-4488 is hsa-miR-4488, miR-1233-5p is hsa-miR-1233-5p, miR-4723-5p is hsa-miR-4723-5p, miR-24-3p is hsa-miR-24-3p, miR-1238-5p is hsa-miR-1238-5p, miR-4442 is hsa-miR-4442, miR-3928-3p is hsa-miR-3928-3p, miR-

6716-5p is hsa-miR-6716-5p, miR-6089 is hsa-miR-6089, miR-6124 is hsa-miR-6124, miR-6778-5p is hsa-miR-6778-5p, miR-557 is hsa-miR-557, and miR-6090 is hsa-miR-6090.

(9) The kit according to (7) or (8), wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (k) to (o):

(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224,

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

(10) The kit according to any one of (1) to (9), wherein the kit comprises at least two or more nucleic acids capable of specifically binding to at least two or more polynucleotides, respectively, selected from all of the liver cancer markers according to (1) or (2).

(11) A device for the detection of liver cancer, comprising nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of liver cancer markers: miR-1343-3p, miR-6726-5p, miR-6515-3p, miR-4651, miR-4257, miR-3188, miR-6131, miR-6766-3p, miR-7641, miR-1249, miR-3679-3p, miR-6787-5p, miR-4454, miR-3135b, miR-6765-3p, miR-7975, miR-204-3p, miR-7977, miR-7110-5p, miR-6717-5p, miR-6870-5p, miR-663b, miR-6875-5p, miR-8072, miR-6816-5p, miR-4281, miR-6729-5p, miR-8069, miR-4706, miR-7108-5p, miR-4433b-3p, miR-6893-5p, miR-6857-5p, miR-1227-5p, miR-6741-5p, miR-451a, miR-8063, miR-3622a-5p, miR-615-5p, miR-128-1-5p, miR-6825-5p, miR-1260b, miR-4433-3p, miR-4665-5p, miR-7845-5p, miR-1908-5p, miR-6840-3p, miR-6765-5p, miR-296-5p, miR-3675-3p, miR-6781-5p, miR-423-5p, miR-3663-3p, miR-6784-5p, miR-6749-5p, miR-1231, miR-4746-3p, miR-6780b-5p, miR-4758-5p, miR-3679-5p, miR-3184-5p, miR-6125, miR-6721-5p, miR-6791-5p, miR-3185, miR-1260a, miR-3197, miR-6845-5p, miR-6887-5p, miR-6738-5p, miR-6872-3p, miR-4497, miR-1229-5p, miR-6820-5p, miR-6777-5p, miR-3917, miR-5787, miR-4286, miR-6877-5p, miR-1225-3p, miR-6088, miR-6800-5p, miR-1246, miR-4467, miR-4419b, miR-1914-3p, miR-4632-5p, miR-1915-5p, miR-3940-5p, miR-1185-2-3p, miR-6746-5p, miR-5001-5p, miR-1228-5p, miR-5572, miR-4327, miR-4638-5p, miR-6799-5p, miR-6861-5p, miR-6727-5p, miR-4513, miR-6805-3p, miR-6808-5p, miR-4449, miR-1199-5p, miR-1275, miR-4792, miR-4443, miR-6891-5p, miR-6826-5p, miR-6807-5p, miR-7150, miR-4534, miR-4476, miR-4649-5p, miR-4525, miR-1915-3p, miR-4516, miR-4417, miR-642b-3p, miR-3141, miR-5100, miR-6848-5p, miR-4739, miR-4459, miR-1237-5p, miR-296-3p, miR-4665-3p, miR-6786-5p, miR-4258, miR-6510-5p, miR-1343-5p, miR-1247-3p, miR-6805-5p, miR-4492, miR-1469, miR-1268b, miR-6858-5p, miR-3937, miR-939-5p, miR-3656, miR-744-5p, miR-4687-3p, miR-4763-3p, miR-3620-5p, miR-3195, miR-6842-5p, miR-4707-5p, miR-642a-3p, miR-7113-3p, miR-4728-5p, miR-5195-3p, miR-1185-1-3p, miR-6774-5p, miR-8059, miR-3131, miR-7847-3p, miR-4463, miR-128-2-5p, miR-4508, miR-6806-5p, miR-7111-5p, miR-6782-5p, miR-4734, miR-3162-5p, miR-887-3p, miR-6752-5p, miR-6724-5p, miR-6757-5p, miR-4448, miR-671-5p, miR-3178, miR-4725-3p, miR-940, miR-6789-5p, miR-4484, miR-4634, miR-4745-5p, miR-4730, miR-6803-5p, miR-6798-5p, miR-3648, miR-4783-3p and miR-6836-3p.

(12) The device according to (11), wherein miR-1343-3p is hsa-miR-1343-3p, miR-6726-5p is hsa-miR-6726-5p, miR-6515-3p is hsa-miR-6515-3p, miR-4651 is hsa-miR-4651, miR-4257 is hsa-miR-4257, miR-3188 is hsa-miR-3188, miR-6131 is hsa-miR-6131, miR-6766-3p is hsa-miR-6766-3p, miR-7641 is hsa-miR-7641, miR-1249 is hsa-miR-1249, miR-3679-3p is hsa-miR-3679-3p, miR-6787-5p is hsa-miR-6787-5p, miR-4454 is hsa-miR-4454, miR-3135b is hsa-miR-3135b, miR-6765-3p is hsa-miR-6765-3p, miR-7975 is hsa-miR-7975, miR-204-3p is hsa-miR-204-3p, miR-7977 is hsa-miR-7977, miR-7110-5p is hsa-miR-7110-5p, miR-6717-5p is hsa-miR-6717-5p, miR-6870-5p is hsa-miR-6870-5p, miR-663b is hsa-miR-663b, miR-6875-5p is hsa-miR-6875-5p, miR-8072 is hsa-miR-8072, miR-6816-5p is hsa-miR-6816-5p, miR-4281 is hsa-miR-4281, miR-6729-5p is hsa-miR-6729-5p, miR-8069 is hsa-miR-8069, miR-4706 is hsa-miR-4706, miR-7108-5p is hsa-miR-7108-5p, miR-4433b-3p is hsa-miR-4433b-3p, miR-6893-5p is hsa-miR-6893-5p, miR-6857-5p is hsa-miR-6857-5p, miR-1227-5p is hsa-miR-1227-5p, miR-6741-5p is hsa-miR-6741-5p, miR-451a is hsa-miR-451a, miR-8063 is hsa-miR-8063, miR-3622a-5p is hsa-miR-3622a-5p, miR-615-5p is hsa-miR-615-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-6825-5p is hsa-miR-6825-5p, miR-1260b is hsa-miR-1260b, miR-4433-3p is hsa-miR-4433-3p, miR-4665-5p is hsa-miR-4665-5p, miR-7845-5p is hsa-miR-7845-5p, miR-1908-5p is hsa-miR-1908-5p, miR-6840-3p is hsa-miR-6840-3p, miR-6765-5p is hsa-miR-6765-5p, miR-296-5p is hsa-miR-296-5p, miR-3675-3p is hsa-miR-3675-3p, miR-6781-5p is hsa-miR-6781-5p, miR-423-5p is hsa-miR-423-5p, miR-3663-3p is hsa-miR-3663-3p, miR-6784-5p is hsa-miR-6784-5p, miR-6749-5p is hsa-miR-6749-5p, miR-1231 is hsa-miR-1231, miR-4746-3p is hsa-miR-4746-3p, miR-6780b-5p is hsa-miR-6780b-5p, miR-4758-5p is hsa-miR-4758-5p, miR-3679-5p is hsa-miR-3679-5p, miR-3184-5p is hsa-miR-3184-5p, miR-6125 is hsa-miR-6125, miR-6721-5p is hsa-miR-6721-5p, miR-6791-5p is hsa-miR-6791-5p, miR-3185 is hsa-miR-3185, miR-1260a is hsa-miR-1260a, miR-3197 is hsa-miR-3197, miR-6845-5p is hsa-miR-6845-5p, miR-6887-5p is hsa-miR-6887-5p, miR-6738-5p is hsa-miR-6738-5p, miR-6872-3p is hsa-miR-6872-3p, miR-4497 is hsa-miR-4497, miR-1229-5p is hsa-miR-1229-5p, miR-6820-5p is hsa-miR-6820-5p, miR-6777-5p is hsa-miR-6777-5p, miR-3917 is hsa-miR-3917, miR-5787 is hsa-miR-5787, miR-4286 is hsa-miR-4286, miR-6877-5p is hsa-miR-6877-5p, miR-1225-3p is hsa-miR-1225-3p, miR-6088 is hsa-miR-6088, miR-6800-5p is hsa-miR-6800-5p, miR-1246 is hsa-miR-1246, miR-4467 is hsa-miR-4467, miR-4419b is hsa-miR-4419b, miR-1914-3p is hsa-miR-1914-3p, miR-4632-5p is hsa-miR-4632-5p, miR-1915-5p is hsa-miR-1915-5p, miR-3940-5p is hsa-miR-3940-5p, miR-1185-2-3p is hsa-miR-1185-2-3p, miR-6746-5p is hsa-miR-6746-5p, miR-5001-5p is hsa-miR-5001-5p, miR-1228-5p is hsa-miR-1228-5p, miR-5572 is hsa-miR-5572, miR-4327 is

hsa-miR-4327, miR-4638-5p is hsa-miR-4638-5p, miR-6799-5p is hsa-miR-6799-5p, miR-6861-5p is hsa-miR-6861-5p, miR-6727-5p is hsa-miR-6727-5p, miR-4513 is hsa-miR-4513, miR-6805-3p is hsa-miR-6805-3p, miR-6808-5p is hsa-miR-6808-5p, miR-4449 is hsa-miR-4449, miR-1199-5p is hsa-miR-1199-5p, miR-1275 is hsa-miR-1275, miR-4792 is hsa-miR-4792, miR-4443 is hsa-miR-4443, miR-6891-5p is hsa-miR-6891-5p, miR-6826-5p is hsa-miR-6826-5p, miR-6807-5p is hsa-miR-6807-5p, miR-7150 is hsa-miR-7150, miR-4534 is hsa-miR-4534, miR-4476 is hsa-miR-4476, miR-4649-5p is hsa-miR-4649-5p, miR-4525 is hsa-miR-4525, miR-1915-3p is hsa-miR-1915-3p, miR-4516 is hsa-miR-4516, miR-4417 is hsa-miR-4417, miR-642b-3p is hsa-miR-642b-3p, miR-3141 is hsa-miR-3141, miR-5100 is hsa-miR-5100, miR-6848-5p is hsa-miR-6848-5p, miR-4739 is hsa-miR-4739, miR-4459 is hsa-miR-4459, miR-1237-5p is hsa-miR-1237-5p, miR-296-3p is hsa-miR-296-3p, miR-4665-3p is hsa-miR-4665-3p, miR-6786-5p is hsa-miR-6786-5p, miR-4258 is hsa-miR-4258, miR-6510-5p is hsa-miR-6510-5p, miR-1343-5p is hsa-miR-1343-5p, miR-1247-3p is hsa-miR-1247-3p, miR-6805-5p is hsa-miR-6805-5p, miR-4492 is hsa-miR-4492, miR-1469 is hsa-miR-1469, miR-1268b is hsa-miR-1268b, miR-6858-5p is hsa-miR-6858-5p, miR-3937 is hsa-miR-3937, miR-939-5p is hsa-miR-939-5p, miR-3656 is hsa-miR-3656, miR-744-5p is hsa-miR-744-5p, miR-4687-3p is hsa-miR-4687-3p, miR-4763-3p is hsa-miR-4763-3p, miR-3620-5p is hsa-miR-3620-5p, miR-3195 is hsa-miR-3195, miR-6842-5p is hsa-miR-6842-5p, miR-4707-5p is hsa-miR-4707-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7113-3p is hsa-miR-7113-3p, miR-4728-5p is hsa-miR-4728-5p, miR-5195-3p is hsa-miR-5195-3p, miR-1185-1-3p is hsa-miR-1185-1-3p, miR-6774-5p is hsa-miR-6774-5p, miR-8059 is hsa-miR-8059, miR-3131 is hsa-miR-3131, miR-7847-3p is hsa-miR-7847-3p, miR-4463 is hsa-miR-4463, miR-128-2-5p is hsa-miR-128-2-5p, miR-4508 is hsa-miR-4508, miR-6806-5p is hsa-miR-6806-5p, miR-7111-5p is hsa-miR-7111-5p, miR-6782-5p is hsa-miR-6782-5p, miR-4734 is hsa-miR-4734, miR-3162-5p is hsa-miR-3162-5p, miR-887-3p is hsa-miR-887-3p, miR-6752-5p is hsa-miR-6752-5p, miR-6724-5p is hsa-miR-6724-5p, miR-6757-5p is hsa-miR-6757-5p, miR-4448 is hsa-miR-4448, miR-671-5p is hsa-miR-671-5p, miR-3178 is hsa-miR-3178, miR-4725-3p is hsa-miR-4725-3p, miR-940 is hsa-miR-940, miR-6789-5p is hsa-miR-6789-5p, miR-4484 is hsa-miR-4484, miR-4634 is hsa-miR-4634, miR-4745-5p is hsa-miR-4745-5p, miR-4730 is hsa-miR-4730, miR-6803-5p is hsa-miR-6803-5p, miR-6798-5p is hsa-miR-6798-5p, miR-3648 is hsa-miR-3648, miR-4783-3p is hsa-miR-4783-3p, and miR-6836-3p is hsa-miR-6836-3p.

(13) The device according to (11) or (12), wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(b) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729,

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

(14) The device according to any of (11) to (13), wherein the device further comprises nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of other liver cancer markers: miR-23b-3p, miR-23a-3p, miR-625-3p, miR-1228-3p, miR-614, miR-1913, miR-92a-2-5p, miR-187-5p, miR-16-5p, miR-92b-3p, miR-150-3p, miR-564, miR-125a-3p, miR-92b-5p, miR-92a-3p and miR-663a.

(15) The device according to (14), wherein miR-23b-3p is hsa-miR-23b-3p, miR-23a-3p is hsa-miR-23a-3p, miR-625-3p is hsa-miR-625-3p, miR-1228-3p is hsa-miR-1228-3p, miR-614 is hsa-miR-614, miR-1913 is hsa-miR-1913, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-187-5p is hsa-miR-187-5p, miR-16-5p is hsa-miR-16-5p, miR-92b-3p is hsa-miR-92b-3p, miR-150-3p is hsa-miR-150-3p, miR-564 is hsa-miR-564, miR-125a-3p is hsa-miR-125a-3p, miR-92b-5p is hsa-miR-92b-5p, miR-92a-3p is hsa-miR-92a-3p, and miR-663a is hsa-miR-663a.

(16) The device according to (14) or (15), wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (f) to (j):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183,

(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i).

(17) The device according to any of (11) to (16), wherein the device further comprises nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of other liver cancer markers: miR-4688, miR-4648, miR-6085, miR-6126, miR-6880-5p, miR-328-5p, miR-6768-5p, miR-3180, miR-6087, miR-1273g-3p, miR-1225-5p, miR-3196, miR-4695-5p, miR-6732-5p, miR-638, miR-6813-5p, miR-665, miR-486-3p, miR-4466, miR-30c-1-3p, miR-3621, miR-6743-5p, miR-4298, miR-4741, miR-3619-3p, miR-6824-5p, miR-5698, miR-371a-5p, miR-4488, miR-1233-5p, miR-4723-5p, miR-24-3p, miR-1238-5p, miR-4442, miR-3928-3p, miR-6716-5p, miR-6089, miR-6124, miR-6778-5p, miR-557 and miR-6090.

(18) The device according to (17), wherein miR-4688 is hsa-miR-4688, miR-4648 is hsa-miR-4648, miR-6085 is hsa-miR-6085, miR-6126 is hsa-miR-6126, miR-6880-5p is hsa-miR-6880-5p, miR-328-5p is hsa-miR-328-5p, miR-6768-5p is hsa-miR-6768-5p, miR-3180 is hsa-miR-3180, miR-6087 is hsa-miR-6087, miR-1273g-3p is hsa-miR-1273g-3p, miR-1225-5p is hsa-miR-1225-5p, miR-3196 is hsa-miR-3196, miR-4695-5p is hsa-miR-4695-5p, miR-6732-5p is hsa-miR-6732-5p, miR-638 is hsa-miR-638, miR-6813-5p is hsa-miR-6813-5p, miR-665 is hsa-miR-665, miR-486-3p is hsa-miR-486-3p, miR-4466 is hsa-miR-4466, miR-30c-1-3p is hsa-miR-30c-1-3p, miR-3621 is hsa-miR-3621, miR-6743-5p is hsa-miR-6743-5p, miR-4298 is hsa-miR-4298, miR-4741 is hsa-miR-4741, miR-3619-3p is hsa-miR-3619-3p, miR-6824-5p is hsa-miR-6824-5p, miR-5698 is hsa-miR-5698, miR-371a-5p is hsa-miR-371a-5p, miR-4488 is hsa-miR-4488, miR-1233-5p is hsa-miR-1233-5p, miR-4723-5p is hsa-miR-4723-5p, miR-24-3p is hsa-miR-24-3p, miR-1238-5p is hsa-miR-1238-5p, miR-4442 is hsa-miR-4442, miR-3928-3p is hsa-miR-3928-3p, miR-6716-5p is hsa-miR-6716-5p, miR-6089 is hsa-miR-6089, miR-6124 is hsa-miR-6124, miR-6778-5p is hsa-miR-6778-5p, miR-557 is hsa-miR-557, and miR-6090 is hsa-miR-6090.

(19) The device according to (17) or (18), wherein the nucleic acid is a polynucleotide selected from the group consisting of the following polynucleotides (k) to (o):

(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224,

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

(20) The device according to any one of (11) to (19), wherein the device is a device for measurement by a hybridization technique.

(21) The device according to (20), wherein the hybridization technique is a nucleic acid array technique.

(22) The device according to any one of (11) to (21), wherein the device comprises at least two or more nucleic acids capable of specifically binding to at least two or more polynucleotides, respectively, selected from all of the liver cancer markers according to (11) or (12).

(23) A method for detecting liver cancer, comprising measuring an expression level of a target nucleic acid in a sample of a subject using the kit according to any one of (1) to (10) or the device according to any one of (11) to (22); and evaluating in vitro whether or not the subject has liver cancer using the measured expression level and a control expression level for a healthy subject measured in the same way.

(24) The method according to (23), wherein the subject is a human.

(25) The method according to (23) or (24), wherein the sample is blood, serum, or plasma.

DEFINITION OF TERM

The terms used herein are defined as follows.

Abbreviations or terms such as nucleotide, polynucleotide, DNA, and RNA abide by "Guidelines for the preparation of specification which contain nucleotide and/or amino acid sequences" (edited by Japan Patent Office) and common use in the art.

The term "polynucleotide" used herein refers to a nucleic acid, including any of RNA, DNA, and RNA/DNA (chimera). The DNA includes any of cDNA, genomic DNA, and synthetic DNA. The RNA includes all of total RNA, mRNA, rRNA, miRNA, siRNA, snoRNA, snRNA, non-coding RNA and synthetic RNA. The "synthetic DNA" and the "synthetic RNA" used herein refer to DNA and RNA artificially prepared using, for example, an automated nucleic acid synthesizer, on the basis of predetermined nucleotide sequences (which may be any of natural and non-natural sequences). The "non-natural sequence" used herein is intended to be used in a broad sense and includes, for example, a sequence containing substitution, deletion, insertion, and/or addition of one or more nucleotide(s) (i.e., a variant sequence) and a sequence containing one or more modified nucleotide(s) (i.e., a modified sequence), which are different from the natural sequence. As used herein, the term "polynucleotide" is used interchangeably with the term "nucleic acid."

The term "fragment" used herein is a polynucleotide having a nucleotide sequence having a consecutive portion of a polynucleotide and desirably has a length of 15 or more nucleotides, preferably 17 or more nucleotides, more preferably 19 or more nucleotides.

The term "gene" used herein is intended to include not only RNA and double-stranded DNA but also each single-stranded DNA such as a plus strand (or a sense strand) or a complementary strand (or an antisense strand) constituting the duplex. The gene is not particularly limited by its length.

Thus, the "gene" used herein includes all of double-stranded DNA including human genomic DNA, single-stranded DNA (plus strand), single-stranded DNA having a sequence complementary to the plus strand (complementary strand) including cDNA, microRNA (miRNA), and their fragments, and transcripts, unless otherwise specified. The "gene" includes not only a "gene" represented by a particular nucleotide sequence (or SEQ ID NO) but "nucleic acids" encoding RNAs having biological functions equivalent to RNA encoded by the gene, for example, a congener (i.e., a homolog or an ortholog), a variant (e.g., a genetic polymorph), and a derivative. Specific examples of such a "nucleic acid" encoding a congener, a variant, or a derivative can include a "nucleic acid" having a nucleotide sequence hybridizing under stringent conditions described later to a complementary sequence of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 765 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t. The "gene" is not particularly limited by its functional region and can contain, for example, an expression regulatory region, a coding region, an exon, or an intron. The "gene" may be contained in a cell or may exist alone after being released into the outside of a cell. Alternatively, the "gene" may be in a state enclosed in a vesicle called exosome.

The term "exosome" used herein is a vesicle that is delimited by a lipid bilayer and secreted from a cell. The

exosome is derived from a multivesicular endosome and may incorporate biomaterials such as "gene(s)" (e.g., RNA or DNA) or protein(s) when released into an extracellular environment. The exosome is known to be contained in a body fluid such as blood, serum, plasma, serum, or lymph.

The term "transcript" used herein refers to RNA synthesized from the DNA sequence of a gene as a template. RNA polymerase binds to a site called a promoter located upstream of the gene and adds ribonucleotides complementary to the nucleotide sequence of the DNA to the 3' end to synthesize RNA. This RNA contains not only the gene itself but also the whole sequence from a transcription initiation site to the end of a polyA sequence, including an expression regulatory region, a coding region, an exon, or an intron.

The term "microRNA (miRNA)" used herein is intended to mean a 15- to 25-nucleotide non-coding RNA that is transcribed as an RNA precursor having a hairpin-like structure, cleaved by a dsRNA-cleaving enzyme which has RNase III cleavage activity, and integrated into a protein complex called RISC, and involved in the suppression of translation of mRNA, unless otherwise specified. The term "miRNA" used herein includes not only a "miRNA" represented by a particular nucleotide sequence (or SEQ ID NO) but a precursor of the "miRNA" (pre-miRNA or pri-miRNA), and miRNAs having biological functions equivalent thereto, for example, a congener (i.e., a homolog or an ortholog), a variant (e.g., a genetic polymorph), and a derivative. Such a precursor, a congener, a variant, or a derivative can be specifically identified using miRBase Release 20 (http://www.mirbase.org/), and examples thereof can include a "miRNA" having a nucleotide sequence hybridizing under stringent conditions described later to a complementary sequence of any particular nucleotide sequence represented by any of SEQ ID NOs: 1 to 765. The term "miRNA" used herein may be a gene product of a miR gene. Such a gene product includes a mature miRNA (e.g., a 15- to 25-nucleotide or 19- to 25-nucleotide non-coding RNA involved in the suppression of translation of mRNA as described above) or a miRNA precursor (e.g., pre-miRNA or pri-miRNA as described above).

The term "probe" used herein includes a polynucleotide that is used for specifically detecting RNA resulting from the expression of a gene or a polynucleotide derived from the RNA, and/or a polynucleotide complementary thereto.

The term "primer" used herein includes a polynucleotide that specifically recognizes and amplifies RNA resulting from the expression of a gene or a polynucleotide derived from the RNA, and/or a polynucleotide complementary thereto.

In this context, the complementary polynucleotide (complementary strand or reverse strand) means a polynucleotide in a complementary relationship of A:T (U) and G:C base pairs with the full-length sequence of a polynucleotide consisting of a nucleotide sequence defined by any of SEQ ID NOs: 1 to 765 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, or a partial sequence thereof (here, this full-length or partial sequence is referred to as a plus strand for the sake of convenience). However, such a complementary strand is not limited to a sequence completely complementary to the nucleotide sequence of the target plus strand and may have a complementary relationship to an extent that permits hybridization under stringent conditions to the target plus strand.

The term "stringent conditions" used herein refers to conditions under which a nucleic acid probe hybridizes to its target sequence to a larger extent (e.g., a measurement value equal to or larger than a mean of background measurement values+a standard deviation of the background measurement values×2) than that for other sequences. The stringent conditions are dependent on a sequence and differ depending on an environment where hybridization is performed. A target sequence that is 100% complementary to the nucleic acid probe can be identified by controlling the stringency of hybridization and/or washing conditions. Specific examples of the "stringent conditions" is mentioned later.

The term "Tm value" used herein means a temperature at which the double-stranded moiety of a polynucleotide is denatured into single strands so that the double strands and the single strands exist at a ratio of 1:1.

The term "variant" used herein means, in the case of a nucleic acid, a natural variant attributed to polymorphism, mutation, or the like; a variant containing the deletion, substitution, addition, or insertion of 1 or 2 or more nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 1 to 765 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, or a partial sequence thereof; a variant that exhibits percent (%) identity of approximately 90% or higher, approximately 95% or higher, approximately 97% or higher, approximately 98% or higher, approximately 99% or higher to each of these nucleotide sequences or the partial sequence thereof; or a nucleic acid hybridizing under the stringent conditions defined above to a polynucleotide or an oligonucleotide comprising each of these nucleotide sequences or the partial sequence thereof.

The term "several" used herein means an integer of approximately 10, 9, 8, 7, 6, 5, 4, 3, or 2.

The variant used herein can be prepared by use of a well-known technique such as site-directed mutagenesis or PCR-based mutagenesis.

The term "percent (%) identity" used herein can be determined with or without an introduced gap, using a protein or gene search system based on BLAST or FASTA described above (Zheng Zhang et al., 2000, J. Comput. Biol., Vol. 7, p. 203-214; Altschul, S. F. et al., 1990, Journal of Molecular Biology, Vol. 215, p. 403-410; and Pearson, W. R. et al., 1988, Proc. Natl. Acad. Sci. U.S.A, Vol. 85, p. 2444-2448).

The term "derivative" used herein is meant to include a modified nucleic acid, for example, a derivative labeled with a fluorophore or the like, a derivative containing a modified nucleotide (e.g., a nucleotide containing a group such as halogen, alkyl such as methyl, alkoxy such as methoxy, thio, or carboxymethyl, and a nucleotide that has undergone base rearrangement, double bond saturation, deamination, replacement of an oxygen molecule with a sulfur atom, etc.), PNA (peptide nucleic acid; Nielsen, P. E. et al., 1991, Science, Vol. 254, p. 1497-500), and LNA (locked nucleic acid; Obika, S. et al., 1998, Tetrahedron Lett., Vol. 39, p. 5401-5404) without any limitation.

As used herein, the "nucleic acid" capable of specifically binding to a polynucleotide selected from the group of the miRNAs described above which are the liver cancer markers is a synthesized or prepared nucleic acid and specifically includes a "nucleic acid probe" or a "primer". The "nucleic acid" is utilized directly or indirectly for detecting the presence or absence of liver cancer in a subject, for diagnosing the presence or absence of liver cancer, the severity of liver cancer, the presence or absence of amelioration or the degree of amelioration of liver cancer, or the therapeutic sensitivity of liver cancer, or for screening for a candidate substance useful in the prevention, amelioration, or treatment of liver cancer. The "nucleic acid" includes a nucleo-

tide, an oligonucleotide, and a polynucleotide capable of specifically recognizing and binding to a transcript represented by any of SEQ ID NOs: 1 to 765 or a synthetic cDNA nucleic acid thereof in vivo, particularly, in a sample such as a body fluid (e.g., blood or urine), in relation to the development of liver cancer. The nucleotide, the oligonucleotide, and the polynucleotide can be effectively used as probes for detecting the aforementioned gene expressed in vivo, in tissues, in cells, or the like on the basis of the properties described above, or as primers for amplifying the aforementioned gene expressed in vivo.

The term "detection" used herein is interchangeable with the term "examination", "measurement", "detection" or "decision support". The term "evaluation" used herein is meant to include diagnosis or evaluation support on the basis of examination results or measurement results.

The term "subject" used herein means a mammal such as a primate including a human and a chimpanzee, a pet animal including a dog and a cat, a livestock animal including cattle, a horse, sheep, and a goat, and a rodent including a mouse and a rat. The term "healthy subject" also means such a mammal without the cancer to be detected.

The term "liver cancer" used herein means "primary liver cancer", which develops primarily in the liver. The liver cancer includes, for example, "hepatocellular carcinoma" and "combined hepatocellular and cholangiocellular carcinoma" caused by the malignant transformation of cells of the liver.

The term "P" or "P value" used herein refers to a probability at which a more extreme statistic than that actually calculated from data under null hypothesis is observed in a statistical test. Thus, smaller "P" or "P value" is regarded as being more significant difference between subjects to be compared.

The term "sensitivity" used herein means a value of (the number of true positives)/(the number of true positives+the number of false negatives). High sensitivity allows liver cancer to be detected early, leading to the complete resection of cancer sites and reduction in the rate of recurrence.

The term "specificity" used herein means a value of (the number of true negatives)/(the number of true negatives+the number of false positives). High specificity prevents needless extra examination for healthy subjects misjudged as being liver cancer patients, leading to reduction in burden on patients and reduction in medical expense.

The term "accuracy" used herein means a value of (the number of true positives+the number of true negatives)/(the total number of cases). The accuracy indicates the ratio of samples that are correctly identified in the discriminant results to all samples, and serves as a primary index for evaluating detection performance.

As used herein, the "sample" that is subjected to determination, detection, or diagnosis refers to a tissue and a biological material in which the expression of the gene of the present invention varies as liver cancer develops, as liver cancer progresses, or as therapeutic effects on liver cancer are exerted. Specifically, the "sample" refers to a hepatic tissue, a perihepatic vascular channel, lymph node, and organ, an organ suspected of having metastasis, the skin, a body fluid such as blood, urine, saliva, sweat, or tissue exudates, serum or plasma prepared from blood, feces, hair, and the like. The "sample" further refers to a biological sample extracted therefrom, specifically, a gene such as RNA or miRNA.

The term "hsa-miR-1343-3p gene" or "hsa-miR-1343-3p" used herein includes the hsa-miR-1343-3p gene (miRBase Accession No. MIMAT0019776) described in SEQ ID NO: 1, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1343-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-1343" (miRBase Accession No. MI0017320, SEQ ID NO: 225) having a hairpin-like structure is known as a precursor of "hsa-miR-1343-3p".

The term "hsa-miR-6726-5p gene" or "hsa-miR-6726-5p" used herein includes the hsa-miR-6726-5p gene (miRBase Accession No. MIMAT0027353) described in SEQ ID NO: 2, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6726-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6726" (miRBase Accession No. MI0022571, SEQ ID NO: 226) having a hairpin-like structure is known as a precursor of "hsa-miR-6726-5p".

The term "hsa-miR-6515-3p gene" or "hsa-miR-6515-3p" used herein includes the hsa-miR-6515-3p gene (miRBase Accession No. MIMAT0025487) described in SEQ ID NO: 3, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6515-3p gene can be obtained by a method described in Joyce C E et al., 2011, Hum Mol Genet, Vol. 20, p. 4025-4040. Also, "hsa-mir-6515" (miRBase Accession No. MI0022227, SEQ ID NO: 227) having a hairpin-like structure is known as a precursor of "hsa-miR-6515-3p".

The term "hsa-miR-4651 gene" or "hsa-miR-4651" used herein includes the hsa-miR-4651 gene (miRBase Accession No. MIMAT0019715) described in SEQ ID NO: 4, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4651 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4651" (miRBase Accession No. MI0017279, SEQ ID NO: 228) having a hairpin-like structure is known as a precursor of "hsa-miR-4651".

The term "hsa-miR-4257 gene" or "hsa-miR-4257" used herein includes the hsa-miR-4257 gene (miRBase Accession No. MIMAT0016878) described in SEQ ID NO: 5, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4257 gene can be obtained by a method described in Goff L A et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4257" (miRBase Accession No. MI0015856, SEQ ID NO: 229) having a hairpin-like structure is known as a precursor of "hsa-miR-4257".

The term "hsa-miR-3188 gene" or "hsa-miR-3188" used herein includes the hsa-miR-3188 gene (miRBase Accession No. MIMAT0015070) described in SEQ ID NO: 6, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3188 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3188" (miRBase Accession No. MI0014232, SEQ ID NO: 230) having a hairpin-like structure is known as a precursor of "hsa-miR-3188".

The term "hsa-miR-6131 gene" or "hsa-miR-6131" used herein includes the hsa-miR-6131 gene (miRBase Accession No. MIMAT0024615) described in SEQ ID NO: 7, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6131 gene can be obtained by a method described in Dannemann M et al., 2012, Genome Biol Evol, Vol. 4, p. 552-564. Also, "hsa-mir-6131" (miRBase Accession No. MI0021276, SEQ ID NO: 231) having a hairpin-like structure is known as a precursor of "hsa-miR-6131".

The term "hsa-miR-6766-3p gene" or "hsa-miR-6766-3p" used herein includes the hsa-miR-6766-3p gene (miRBase Accession No. MIMAT0027433) described in SEQ ID NO: 8, a homolog or an ortholog of a different organism species,

and the like. The hsa-miR-6766-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6766" (miRBase Accession No. MI0022611, SEQ ID NO: 232) having a hairpin-like structure is known as a precursor of "hsa-miR-6766-3p".

The term "hsa-miR-7641 gene" or "hsa-miR-7641" used herein includes the hsa-miR-7641 gene (miRBase Accession No. MIMAT0029782) described in SEQ ID NO: 9, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7641 gene can be obtained by a method described in Yoo J K et al., 2013, Arch Pharm Res, Vol. 36, p. 353-358. Also, "hsa-mir-7641-1" and "hsa-mir-7641-2" (miRBase Accession Nos. MI0024975 and MI0024976, SEQ ID NOs: 233 and 234) having a hairpin-like structure are known as precursors of "hsa-miR-7641".

The term "hsa-miR-1249 gene" or "hsa-miR-1249" used herein includes the hsa-miR-1249 gene (miRBase Accession No. MIMAT0005901) described in SEQ ID NO: 10, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1249 gene can be obtained by a method described in Morin R D et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1249" (miRBase Accession No. MI0006384, SEQ ID NO: 235) having a hairpin-like structure is known as a precursor of "hsa-miR-1249".

The term "hsa-miR-3679-3p gene" or "hsa-miR-3679-3p" used herein includes the hsa-miR-3679-3p gene (miRBase Accession No. MIMAT0018105) described in SEQ ID NO: 11, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3679-3p gene can be obtained by a method described in Creighton C J et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3679" (miRBase Accession No. MI0016080, SEQ ID NO: 236) having a hairpin-like structure is known as a precursor of "hsa-miR-3679-3p".

The term "hsa-miR-6787-5p gene" or "hsa-miR-6787-5p" used herein includes the hsa-miR-6787-5p gene (miRBase Accession No. MIMAT0027474) described in SEQ ID NO: 12, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6787-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6787" (miRBase Accession No. MI0022632, SEQ ID NO: 237) having a hairpin-like structure is known as a precursor of "hsa-miR-6787-5p".

The term "hsa-miR-4454 gene" or "hsa-miR-4454" used herein includes the hsa-miR-4454 gene (miRBase Accession No. MIMAT0018976) described in SEQ ID NO: 13, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4454 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4454" (miRBase Accession No. MI0016800, SEQ ID NO: 238) having a hairpin-like structure is known as a precursor of "hsa-miR-4454".

The term "hsa-miR-3135b gene" or "hsa-miR-3135b" used herein includes the hsa-miR-3135b gene (miRBase Accession No. MIMAT0018985) described in SEQ ID NO: 14, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3135b gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-3135b" (miRBase Accession No. MI0016809, SEQ ID NO: 239) having a hairpin-like structure is known as a precursor of "hsa-miR-3135b".

The term "hsa-miR-6765-3p gene" or "hsa-miR-6765-3p" used herein includes the hsa-miR-6765-3p gene (miRBase Accession No. MIMAT0027431) described in SEQ ID NO: 15, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6765-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6765" (miRBase Accession No. MI0022610, SEQ ID NO: 240) having a hairpin-like structure is known as a precursor of "hsa-miR-6765-3p".

The term "hsa-miR-7975 gene" or "hsa-miR-7975" used herein includes the hsa-miR-7975 gene (miRBase Accession No. MIMAT0031178) described in SEQ ID NO: 16, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7975 gene can be obtained by a method described in Velthut-Meikas A et al., 2013, Mol Endocrinol, online. Also, "hsa-mir-7975" (miRBase Accession No. MI0025751, SEQ ID NO: 241) having a hairpin-like structure is known as a precursor of "hsa-miR-7975".

The term "hsa-miR-204-3p gene" or "hsa-miR-204-3p" used herein includes the hsa-miR-204-3p gene (miRBase Accession No. MIMAT0022693) described in SEQ ID NO: 17, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-204-3p gene can be obtained by a method described in Lim L P et al., 2003, Science, Vol. 299, p. 1540. Also, "hsa-mir-204" (miRBase Accession No. MI0000284, SEQ ID NO: 242) having a hairpin-like structure is known as a precursor of "hsa-miR-204-3p".

The term "hsa-miR-7977 gene" or "hsa-miR-7977" used herein includes the hsa-miR-7977 gene (miRBase Accession No. MIMAT0031180) described in SEQ ID NO: 18, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7977 gene can be obtained by a method described in Velthut-Meikas A et al., 2013, Mol Endocrinol, online. Also, "hsa-mir-7977" (miRBase Accession No. MI0025753, SEQ ID NO: 243) having a hairpin-like structure is known as a precursor of "hsa-miR-7977".

The term "hsa-miR-7110-5p gene" or "hsa-miR-7110-5p" used herein includes the hsa-miR-7110-5p gene (miRBase Accession No. MIMAT0028117) described in SEQ ID NO: 19, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7110-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7110" (miRBase Accession No. MI0022961, SEQ ID NO: 244) having a hairpin-like structure is known as a precursor of "hsa-miR-7110-5p".

The term "hsa-miR-6717-5p gene" or "hsa-miR-6717-5p" used herein includes the hsa-miR-6717-5p gene (miRBase Accession No. MIMAT0025846) described in SEQ ID NO: 20, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6717-5p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6717" (miRBase Accession No. MI0022551, SEQ ID NO: 245) having a hairpin-like structure is known as a precursor of "hsa-miR-6717-5p".

The term "hsa-miR-6870-5p gene" or "hsa-miR-6870-5p" used herein includes the hsa-miR-6870-5p gene (miRBase Accession No. MIMAT0027640) described in SEQ ID NO: 21, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6870-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6870" (miRBase Accession No. MI0022717, SEQ ID NO: 246) having a hairpin-like structure is known as a precursor of "hsa-miR-6870-5p".

The term "hsa-miR-663b gene" or "hsa-miR-663b" used herein includes the hsa-miR-663b gene (miRBase Accession No. MIMAT0005867) described in SEQ ID NO: 22, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-663b gene can be obtained by a method described in Takada S et al., 2008, Leukemia, Vol.

22, p. 1274-1278. Also, "hsa-mir-663b" (miRBase Accession No. MI0006336, SEQ ID NO: 247) having a hairpin-like structure is known as a precursor of "hsa-miR-663b".

The term "hsa-miR-6875-5p gene" or "hsa-miR-6875-5p" used herein includes the hsa-miR-6875-5p gene (miRBase Accession No. MIMAT0027650) described in SEQ ID NO: 23, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6875-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6875" (miRBase Accession No. MI0022722, SEQ ID NO: 248) having a hairpin-like structure is known as a precursor of "hsa-miR-6875-5p".

The term "hsa-miR-8072 gene" or "hsa-miR-8072" used herein includes the hsa-miR-8072 gene (miRBase Accession No. MIMAT0030999) described in SEQ ID NO: 24, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8072 gene can be obtained by a method described in Wang H J et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8072" (miRBase Accession No. MI0025908, SEQ ID NO: 249) having a hairpin-like structure is known as a precursor of "hsa-miR-8072".

The term "hsa-miR-6816-5p gene" or "hsa-miR-6816-5p" used herein includes the hsa-miR-6816-5p gene (miRBase Accession No. MIMAT0027532) described in SEQ ID NO: 25, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6816-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6816" (miRBase Accession No. MI0022661, SEQ ID NO: 250) having a hairpin-like structure is known as a precursor of "hsa-miR-6816-5p".

The term "hsa-miR-4281 gene" or "hsa-miR-4281" used herein includes the hsa-miR-4281 gene (miRBase Accession No. MIMAT0016907) described in SEQ ID NO: 26, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4281 gene can be obtained by a method described in Goff L A et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4281" (miRBase Accession No. MI0015885, SEQ ID NO: 251) having a hairpin-like structure is known as a precursor of "hsa-miR-4281".

The term "hsa-miR-6729-5p gene" or "hsa-miR-6729-5p" used herein includes the hsa-miR-6729-5p gene (miRBase Accession No. MIMAT0027359) described in SEQ ID NO: 27, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6729-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6729" (miRBase Accession No. MI0022574, SEQ ID NO: 252) having a hairpin-like structure is known as a precursor of "hsa-miR-6729-5p".

The term "hsa-miR-8069 gene" or "hsa-miR-8069" used herein includes the hsa-miR-8069 gene (miRBase Accession No. MIMAT0030996) described in SEQ ID NO: 28, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8069 gene can be obtained by a method described in Wang H J et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8069" (miRBase Accession No. MI0025905, SEQ ID NO: 253) having a hairpin-like structure is known as a precursor of "hsa-miR-8069".

The term "hsa-miR-4706 gene" or "hsa-miR-4706" used herein includes the hsa-miR-4706 gene (miRBase Accession No. MIMAT0019806) described in SEQ ID NO: 29, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4706 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4706" (miRBase Accession No. MI0017339, SEQ ID NO: 254) having a hairpin-like structure is known as a precursor of "hsa-miR-4706".

The term "hsa-miR-7108-5p gene" or "hsa-miR-7108-5p" used herein includes the hsa-miR-7108-5p gene (miRBase Accession No. MIMAT0028113) described in SEQ ID NO: 30, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7108-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7108" (miRBase Accession No. MI0022959, SEQ ID NO: 255) having a hairpin-like structure is known as a precursor of "hsa-miR-7108-5p".

The term "hsa-miR-4433b-3p gene" or "hsa-miR-4433b-3p" used herein includes the hsa-miR-4433b-3p gene (miRBase Accession No. MIMAT0030414) described in SEQ ID NO: 31, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4433b-3p gene can be obtained by a method described in Ple H et al., 2012, PLoS One, Vol. 7, e50746. Also, "hsa-mir-4433b" (miRBase Accession No. MI0025511, SEQ ID NO: 256) having a hairpin-like structure is known as a precursor of "hsa-miR-4433b-3p".

The term "hsa-miR-6893-5p gene" or "hsa-miR-6893-5p" used herein includes the hsa-miR-6893-5p gene (miRBase Accession No. MIMAT0027686) described in SEQ ID NO: 32, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6893-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6893" (miRBase Accession No. MI0022740, SEQ ID NO: 257) having a hairpin-like structure is known as a precursor of "hsa-miR-6893-5p".

The term "hsa-miR-6857-5p gene" or "hsa-miR-6857-5p" used herein includes the hsa-miR-6857-5p gene (miRBase Accession No. MIMAT0027614) described in SEQ ID NO: 33, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6857-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6857" (miRBase Accession No. MI0022703, SEQ ID NO: 258) having a hairpin-like structure is known as a precursor of "hsa-miR-6857-5p".

The term "hsa-miR-1227-5p gene" or "hsa-miR-1227-5p" used herein includes the hsa-miR-1227-5p gene (miRBase Accession No. MIMAT0022941) described in SEQ ID NO: 34, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1227-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1227" (miRBase Accession No. MI0006316, SEQ ID NO: 259) having a hairpin-like structure is known as a precursor of "hsa-miR-1227-5p".

The term "hsa-miR-6741-5p gene" or "hsa-miR-6741-5p" used herein includes the hsa-miR-6741-5p gene (miRBase Accession No. MIMAT0027383) described in SEQ ID NO: 35, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6741-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6741" (miRBase Accession No. MI0022586, SEQ ID NO: 260) having a hairpin-like structure is known as a precursor of "hsa-miR-6741-5p".

The term "hsa-miR-451a gene" or "hsa-miR-451a" used herein includes the hsa-miR-451a gene (miRBase Accession No. MIMAT0001631) described in SEQ ID NO: 36, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-451a gene can be obtained by a

method described in Altuvia Y et al., 2005, Nucleic Acids Res, Vol. 33, p. 2697-2706. Also, "hsa-mir-451a" (miRBase Accession No. MI0001729, SEQ ID NO: 261) having a hairpin-like structure is known as a precursor of "hsa-miR-451a".

The term "hsa-miR-8063 gene" or "hsa-miR-8063" used herein includes the hsa-miR-8063 gene (miRBase Accession No. MIMAT0030990) described in SEQ ID NO: 37, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8063 gene can be obtained by a method described in Wang H J et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8063" (miRBase Accession No. MI0025899, SEQ ID NO: 262) having a hairpin-like structure is known as a precursor of "hsa-miR-8063".

The term "hsa-miR-3622a-5p gene" or "hsa-miR-3622a-5p" used herein includes the hsa-miR-3622a-5p gene (miRBase Accession No. MIMAT0018003) described in SEQ ID NO: 38, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3622a-5p gene can be obtained by a method described in Witten D et al., 2010, BMC Biol, Vol. 8, p. 58. Also, "hsa-mir-3622a" (miRBase Accession No. MI0016013, SEQ ID NO: 263) having a hairpin-like structure is known as a precursor of "hsa-miR-3622a-5p".

The term "hsa-miR-615-5p gene" or "hsa-miR-615-5p" used herein includes the hsa-miR-615-5p gene (miRBase Accession No. MIMAT0004804) described in SEQ ID NO: 39, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-615-5p gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-615" (miRBase Accession No. MI0003628, SEQ ID NO: 264) having a hairpin-like structure is known as a precursor of "hsa-miR-615-5p".

The term "hsa-miR-128-1-5p gene" or "hsa-miR-128-1-5p" used herein includes the hsa-miR-128-1-5p gene (miRBase Accession No. MIMAT0026477) described in SEQ ID NO: 40, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-128-1-5p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-128-1" (miRBase Accession No. MI0000447, SEQ ID NO: 265) having a hairpin-like structure is known as a precursor of "hsa-miR-128-1-5p".

The term "hsa-miR-6825-5p gene" or "hsa-miR-6825-5p" used herein includes the hsa-miR-6825-5p gene (miRBase Accession No. MIMAT0027550) described in SEQ ID NO: 41, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6825-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6825" (miRBase Accession No. MI0022670, SEQ ID NO: 266) having a hairpin-like structure is known as a precursor of "hsa-miR-6825-5p".

The term "hsa-miR-1260b gene" or "hsa-miR-1260b" used herein includes the hsa-miR-1260b gene (miRBase Accession No. MIMAT0015041) described in SEQ ID NO: 42, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1260b gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-1260b" (miRBase Accession No. MI0014197, SEQ ID NO: 267) having a hairpin-like structure is known as a precursor of "hsa-miR-1260b".

The term "hsa-miR-4433-3p gene" or "hsa-miR-4433-3p" used herein includes the hsa-miR-4433-3p gene (miRBase Accession No. MIMAT0018949) described in SEQ ID NO: 43, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4433-3p gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4433" (miRBase Accession No. MI0016773, SEQ ID NO: 268) having a hairpin-like structure is known as a precursor of "hsa-miR-4433-3p".

The term "hsa-miR-4665-5p gene" or "hsa-miR-4665-5p" used herein includes the hsa-miR-4665-5p gene (miRBase Accession No. MIMAT0019739) described in SEQ ID NO: 44, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4665-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4665" (miRBase Accession No. MI0017295, SEQ ID NO: 269) having a hairpin-like structure is known as a precursor of "hsa-miR-4665-5p".

The term "hsa-miR-7845-5p gene" or "hsa-miR-7845-5p" used herein includes the hsa-miR-7845-5p gene (miRBase Accession No. MIMAT0030420) described in SEQ ID NO: 45, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7845-5p gene can be obtained by a method described in Ple H et al., 2012, PLoS One, Vol. 7, e50746. Also, "hsa-mir-7845" (miRBase Accession No. MI0025515, SEQ ID NO: 270) having a hairpin-like structure is known as a precursor of "hsa-miR-7845-5p".

The term "hsa-miR-1908-5p gene" or "hsa-miR-1908-5p" used herein includes the hsa-miR-1908-5p gene (miRBase Accession No. MIMAT0007881) described in SEQ ID NO: 46, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1908-5p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1908" (miRBase Accession No. MI0008329, SEQ ID NO: 271) having a hairpin-like structure is known as a precursor of "hsa-miR-1908-5p".

The term "hsa-miR-6840-3p gene" or "hsa-miR-6840-3p" used herein includes the hsa-miR-6840-3p gene (miRBase Accession No. MIMAT0027583) described in SEQ ID NO: 47, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6840-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6840" (miRBase Accession No. MI0022686, SEQ ID NO: 272) having a hairpin-like structure is known as a precursor of "hsa-miR-6840-3p".

The term "hsa-miR-6765-5p gene" or "hsa-miR-6765-5p" used herein includes the hsa-miR-6765-5p gene (miRBase Accession No. MIMAT0027430) described in SEQ ID NO: 48, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6765-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6765" (miRBase Accession No. MI0022610, SEQ ID NO: 240) having a hairpin-like structure is known as a precursor of "hsa-miR-6765-5p".

The term "hsa-miR-296-5p gene" or "hsa-miR-296-5p" used herein includes the hsa-miR-296-5p gene (miRBase Accession No. MIMAT0000690) described in SEQ ID NO: 49, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-296-5p gene can be obtained by a method described in Houbaviy H B et al., 2003, Dev Cell, Vol. 5, p. 351-358. Also, "hsa-mir-296" (miRBase Accession No. MI0000747, SEQ ID NO: 273) having a hairpin-like structure is known as a precursor of "hsa-miR-296-5p".

The term "hsa-miR-3675-3p gene" or "hsa-miR-3675-3p" used herein includes the hsa-miR-3675-3p gene (miRBase Accession No. MIMAT0018099) described in SEQ ID NO: 50, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3675-3p gene can be obtained by

a method described in Vaz C et al., 2010, BMC Genomics, Vol. 11, p. 288. Also, "hsa-mir-3675" (miRBase Accession No. MI0016076, SEQ ID NO: 274) having a hairpin-like structure is known as a precursor of "hsa-miR-3675-3p".

The term "hsa-miR-6781-5p gene" or "hsa-miR-6781-5p" used herein includes the hsa-miR-6781-5p gene (miRBase Accession No. MIMAT0027462) described in SEQ ID NO: 51, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6781-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6781" (miRBase Accession No. MI0022626, SEQ ID NO: 275) having a hairpin-like structure is known as a precursor of "hsa-miR-6781-5p".

The term "hsa-miR-423-5p gene" or "hsa-miR-423-5p" used herein includes the hsa-miR-423-5p gene (miRBase Accession No. MIMAT0004748) described in SEQ ID NO: 52, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-423-5p gene can be obtained by a method described in Kasashima K et al., 2004, Biochem Biophys Res Commun, Vol. 322, p. 403-410. Also, "hsa-mir-423" (miRBase Accession No. MI0001445, SEQ ID NO: 276) having a hairpin-like structure is known as a precursor of "hsa-miR-423-5p".

The term "hsa-miR-3663-3p gene" or "hsa-miR-3663-3p" used herein includes the hsa-miR-3663-3p gene (miRBase Accession No. MIMAT0018085) described in SEQ ID NO: 53, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3663-3p gene can be obtained by a method described in Liao J Y et al., 2010, PLoS One, Vol. 5, e10563. Also, "hsa-mir-3663" (miRBase Accession No. MI0016064, SEQ ID NO: 277) having a hairpin-like structure is known as a precursor of "hsa-miR-3663-3p".

The term "hsa-miR-6784-5p gene" or "hsa-miR-6784-5p" used herein includes the hsa-miR-6784-5p gene (miRBase Accession No. MIMAT0027468) described in SEQ ID NO: 54, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6784-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6784" (miRBase Accession No. MI0022629, SEQ ID NO: 278) having a hairpin-like structure is known as a precursor of "hsa-miR-6784-5p".

The term "hsa-miR-6749-5p gene" or "hsa-miR-6749-5p" used herein includes the hsa-miR-6749-5p gene (miRBase Accession No. MIMAT0027398) described in SEQ ID NO: 55, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6749-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6749" (miRBase Accession No. MI0022594, SEQ ID NO: 279) having a hairpin-like structure is known as a precursor of "hsa-miR-6749-5p".

The term "hsa-miR-1231 gene" or "hsa-miR-1231" used herein includes the hsa-miR-1231 gene (miRBase Accession No. MIMAT0005586) described in SEQ ID NO: 56, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1231 gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1231" (miRBase Accession No. MI0006321, SEQ ID NO: 280) having a hairpin-like structure is known as a precursor of "hsa-miR-1231".

The term "hsa-miR-4746-3p gene" or "hsa-miR-4746-3p" used herein includes the hsa-miR-4746-3p gene (miRBase Accession No. MIMAT0019881) described in SEQ ID NO: 57, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4746-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4746" (miRBase Accession No. MI0017385, SEQ ID NO: 281) having a hairpin-like structure is known as a precursor of "hsa-miR-4746-3p".

The term "hsa-miR-6780b-5p gene" or "hsa-miR-6780b-5p" used herein includes the hsa-miR-6780b-5p gene (miRBase Accession No. MIMAT0027572) described in SEQ ID NO: 58, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6780b-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6780b" (miRBase Accession No. MI0022681, SEQ ID NO: 282) having a hairpin-like structure is known as a precursor of "hsa-miR-6780b-5p".

The term "hsa-miR-4758-5p gene" or "hsa-miR-4758-5p" used herein includes the hsa-miR-4758-5p gene (miRBase Accession No. MIMAT0019903) described in SEQ ID NO: 59, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4758-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4758" (miRBase Accession No. MI0017399, SEQ ID NO: 283) having a hairpin-like structure is known as a precursor of "hsa-miR-4758-5p".

The term "hsa-miR-3679-5p gene" or "hsa-miR-3679-5p" used herein includes the hsa-miR-3679-5p gene (miRBase Accession No. MIMAT0018104) described in SEQ ID NO: 60, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3679-5p gene can be obtained by a method described in Creighton C J et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3679" (miRBase Accession No. MI0016080, SEQ ID NO: 236) having a hairpin-like structure is known as a precursor of "hsa-miR-3679-5p".

The term "hsa-miR-3184-5p gene" or "hsa-miR-3184-5p" used herein includes the hsa-miR-3184-5p gene (miRBase Accession No. MIMAT0015064) described in SEQ ID NO: 61, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3184-5p gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3184" (miRBase Accession No. MI0014226, SEQ ID NO: 284) having a hairpin-like structure is known as a precursor of "hsa-miR-3184-5p".

The term "hsa-miR-6125 gene" or "hsa-miR-6125" used herein includes the hsa-miR-6125 gene (miRBase Accession No. MIMAT0024598) described in SEQ ID NO: 62, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6125 gene can be obtained by a method described in Smith J L et al., 2012, J Virol, Vol. 86, p. 5278-5287. Also, "hsa-mir-6125" (miRBase Accession No. MI0021259, SEQ ID NO: 285) having a hairpin-like structure is known as a precursor of "hsa-miR-6125".

The term "hsa-miR-6721-5p gene" or "hsa-miR-6721-5p" used herein includes the hsa-miR-6721-5p gene (miRBase Accession No. MIMAT0025852) described in SEQ ID NO: 63, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6721-5p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6721" (miRBase Accession No. MI0022556, SEQ ID NO: 286) having a hairpin-like structure is known as a precursor of "hsa-miR-6721-5p".

The term "hsa-miR-6791-5p gene" or "hsa-miR-6791-5p" used herein includes the hsa-miR-6791-5p gene (miRBase Accession No. MIMAT0027482) described in SEQ ID NO: 64, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6791-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6791" (miRBase

Accession No. MI0022636, SEQ ID NO: 287) having a hairpin-like structure is known as a precursor of "hsa-miR-6791-5p".

The term "hsa-miR-3185 gene" or "hsa-miR-3185" used herein includes the hsa-miR-3185 gene (miRBase Accession No. MIMAT0015065) described in SEQ ID NO: 65, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3185 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3185" (miRBase Accession No. MI0014227, SEQ ID NO: 288) having a hairpin-like structure is known as a precursor of "hsa-miR-3185".

The term "hsa-miR-1260a gene" or "hsa-miR-1260a" used herein includes the hsa-miR-1260a gene (miRBase Accession No. MIMAT0005911) described in SEQ ID NO: 66, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1260a gene can be obtained by a method described in Morin R D et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1260a" (miRBase Accession No. MI0006394, SEQ ID NO: 289) having a hairpin-like structure is known as a precursor of "hsa-miR-1260a".

The term "hsa-miR-3197 gene" or "hsa-miR-3197" used herein includes the hsa-miR-3197 gene (miRBase Accession No. MIMAT0015082) described in SEQ ID NO: 67, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3197 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3197" (miRBase Accession No. MI0014245, SEQ ID NO: 290) having a hairpin-like structure is known as a precursor of "hsa-miR-3197".

The term "hsa-miR-6845-5p gene" or "hsa-miR-6845-5p" used herein includes the hsa-miR-6845-5p gene (miRBase Accession No. MIMAT0027590) described in SEQ ID NO: 68, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6845-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6845" (miRBase Accession No. MI0022691, SEQ ID NO: 291) having a hairpin-like structure is known as a precursor of "hsa-miR-6845-5p".

The term "hsa-miR-6887-5p gene" or "hsa-miR-6887-5p" used herein includes the hsa-miR-6887-5p gene (miRBase Accession No. MIMAT0027674) described in SEQ ID NO: 69, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6887-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6887" (miRBase Accession No. MI0022734, SEQ ID NO: 292) having a hairpin-like structure is known as a precursor of "hsa-miR-6887-5p".

The term "hsa-miR-6738-5p gene" or "hsa-miR-6738-5p" used herein includes the hsa-miR-6738-5p gene (miRBase Accession No. MIMAT0027377) described in SEQ ID NO: 70, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6738-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6738" (miRBase Accession No. MI0022583, SEQ ID NO: 293) having a hairpin-like structure is known as a precursor of "hsa-miR-6738-5p".

The term "hsa-miR-6872-3p gene" or "hsa-miR-6872-3p" used herein includes the hsa-miR-6872-3p gene (miRBase Accession No. MIMAT0027645) described in SEQ ID NO: 71, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6872-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6872" (miRBase Accession No. MI0022719, SEQ ID NO: 294) having a hairpin-like structure is known as a precursor of "hsa-miR-6872-3p".

The term "hsa-miR-4497 gene" or "hsa-miR-4497" used herein includes the hsa-miR-4497 gene (miRBase Accession No. MIMAT0019032) described in SEQ ID NO: 72, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4497 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4497" (miRBase Accession No. MI0016859, SEQ ID NO: 295) having a hairpin-like structure is known as a precursor of "hsa-miR-4497".

The term "hsa-miR-1229-5p gene" or "hsa-miR-1229-5p" used herein includes the hsa-miR-1229-5p gene (miRBase Accession No. MIMAT0022942) described in SEQ ID NO: 73, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1229-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1229" (miRBase Accession No. MI0006319, SEQ ID NO: 296) having a hairpin-like structure is known as a precursor of "hsa-miR-1229-5p".

The term "hsa-miR-6820-5p gene" or "hsa-miR-6820-5p" used herein includes the hsa-miR-6820-5p gene (miRBase Accession No. MIMAT0027540) described in SEQ ID NO: 74, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6820-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6820" (miRBase Accession No. MI0022665, SEQ ID NO: 297) having a hairpin-like structure is known as a precursor of "hsa-miR-6820-5p".

The term "hsa-miR-6777-5p gene" or "hsa-miR-6777-5p" used herein includes the hsa-miR-6777-5p gene (miRBase Accession No. MIMAT0027454) described in SEQ ID NO: 75, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6777-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6777" (miRBase Accession No. MI0022622, SEQ ID NO: 298) having a hairpin-like structure is known as a precursor of "hsa-miR-6777-5p".

The term "hsa-miR-3917 gene" or "hsa-miR-3917" used herein includes the hsa-miR-3917 gene (miRBase Accession No. MIMAT0018191) described in SEQ ID NO: 76, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3917 gene can be obtained by a method described in Creighton C J et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3917" (miRBase Accession No. MI0016423, SEQ ID NO: 299) having a hairpin-like structure is known as a precursor of "hsa-miR-3917".

The term "hsa-miR-5787 gene" or "hsa-miR-5787" used herein includes the hsa-miR-5787 gene (miRBase Accession No. MIMAT0023252) described in SEQ ID NO: 77, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5787 gene can be obtained by a method described in Yoo H et al., 2011, Biochem Biophys Res Commun, Vol. 415, p. 567-572. Also, "hsa-mir-5787" (miRBase Accession No. MI0019797, SEQ ID NO: 300) having a hairpin-like structure is known as a precursor of "hsa-miR-5787".

The term "hsa-miR-4286 gene" or "hsa-miR-4286" used herein includes the hsa-miR-4286 gene (miRBase Accession No. MIMAT0016916) described in SEQ ID NO: 78, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4286 gene can be obtained by a

method described in Goff L A et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4286" (miRBase Accession No. MI0015894, SEQ ID NO: 301) having a hairpin-like structure is known as a precursor of "hsa-miR-4286".

The term "hsa-miR-6877-5p gene" or "hsa-miR-6877-5p" used herein includes the hsa-miR-6877-5p gene (miRBase Accession No. MIMAT0027654) described in SEQ ID NO: 79, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6877-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6877" (miRBase Accession No. MI0022724, SEQ ID NO: 302) having a hairpin-like structure is known as a precursor of "hsa-miR-6877-5p".

The term "hsa-miR-1225-3p gene" or "hsa-miR-1225-3p" used herein includes the hsa-miR-1225-3p gene (miRBase Accession No. MIMAT0005573) described in SEQ ID NO: 80, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1225-3p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1225" (miRBase Accession No. MI0006311, SEQ ID NO: 303) having a hairpin-like structure is known as a precursor of "hsa-miR-1225-3p".

The term "hsa-miR-6088 gene" or "hsa-miR-6088" used herein includes the hsa-miR-6088 gene (miRBase Accession No. MIMAT0023713) described in SEQ ID NO: 81, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6088 gene can be obtained by a method described in Yoo J K et al., 2012, Stem Cells Dev, Vol. 21, p. 2049-2057. Also, "hsa-mir-6088" (miRBase Accession No. MI0020365, SEQ ID NO: 304) having a hairpin-like structure is known as a precursor of "hsa-miR-6088".

The term "hsa-miR-6800-5p gene" or "hsa-miR-6800-5p" used herein includes the hsa-miR-6800-5p gene (miRBase Accession No. MIMAT0027500) described in SEQ ID NO: 82, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6800-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6800" (miRBase Accession No. MI0022645, SEQ ID NO: 305) having a hairpin-like structure is known as a precursor of "hsa-miR-6800-5p".

The term "hsa-miR-1246 gene" or "hsa-miR-1246" used herein includes the hsa-miR-1246 gene (miRBase Accession No. MIMAT0005898) described in SEQ ID NO: 83, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1246 gene can be obtained by a method described in Morin R D et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1246" (miRBase Accession No. MI0006381, SEQ ID NO: 306) having a hairpin-like structure is known as a precursor of "hsa-miR-1246".

The term "hsa-miR-4467 gene" or "hsa-miR-4467" used herein includes the hsa-miR-4467 gene (miRBase Accession No. MIMAT0018994) described in SEQ ID NO: 84, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4467 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4467" (miRBase Accession No. MI0016818, SEQ ID NO: 307) having a hairpin-like structure is known as a precursor of "hsa-miR-4467".

The term "hsa-miR-4419b gene" or "hsa-miR-4419b" used herein includes the hsa-miR-4419b gene (miRBase Accession No. MIMAT0019034) described in SEQ ID NO: 85, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4419b gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4419b" (miRBase Accession No. MI0016861, SEQ ID NO: 308) having a hairpin-like structure is known as a precursor of "hsa-miR-4419b".

The term "hsa-miR-1914-3p gene" or "hsa-miR-1914-3p" used herein includes the hsa-miR-1914-3p gene (miRBase Accession No. MIMAT0007890) described in SEQ ID NO: 86, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1914-3p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1914" (miRBase Accession No. MI0008335, SEQ ID NO: 309) having a hairpin-like structure is known as a precursor of "hsa-miR-1914-3p".

The term "hsa-miR-4632-5p gene" or "hsa-miR-4632-5p" used herein includes the hsa-miR-4632-5p gene (miRBase Accession No. MIMAT0022977) described in SEQ ID NO: 87, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4632-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4632" (miRBase Accession No. MI0017259, SEQ ID NO: 310) having a hairpin-like structure is known as a precursor of "hsa-miR-4632-5p".

The term "hsa-miR-1915-5p gene" or "hsa-miR-1915-5p" used herein includes the hsa-miR-1915-5p gene (miRBase Accession No. MIMAT0007891) described in SEQ ID NO: 88, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1915-5p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1915" (miRBase Accession No. MI0008336, SEQ ID NO: 311) having a hairpin-like structure is known as a precursor of "hsa-miR-1915-5p".

The term "hsa-miR-3940-5p gene" or "hsa-miR-3940-5p" used herein includes the hsa-miR-3940-5p gene (miRBase Accession No. MIMAT0019229) described in SEQ ID NO: 89, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3940-5p gene can be obtained by a method described in Liao J Y et al., 2010, PLoS One, Vol. 5, e10563. Also, "hsa-mir-3940" (miRBase Accession No. MI0016597, SEQ ID NO: 312) having a hairpin-like structure is known as a precursor of "hsa-miR-3940-5p".

The term "hsa-miR-1185-2-3p gene" or "hsa-miR-1185-2-3p" used herein includes the hsa-miR-1185-2-3p gene (miRBase Accession No. MIMAT0022713) described in SEQ ID NO: 90, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1185-2-3p gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-1185-2" (miRBase Accession No. MI0003821, SEQ ID NO: 313) having a hairpin-like structure is known as a precursor of "hsa-miR-1185-2-3p".

The term "hsa-miR-6746-5p gene" or "hsa-miR-6746-5p" used herein includes the hsa-miR-6746-5p gene (miRBase Accession No. MIMAT0027392) described in SEQ ID NO: 91, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6746-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6746" (miRBase Accession No. MI0022591, SEQ ID NO: 314) having a hairpin-like structure is known as a precursor of "hsa-miR-6746-5p".

The term "hsa-miR-5001-5p gene" or "hsa-miR-5001-5p" used herein includes the hsa-miR-5001-5p gene (miRBase Accession No. MIMAT0021021) described in SEQ ID NO: 92, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5001-5p gene can be obtained by

a method described in Hansen T B et al., 2011, RNA Biol, Vol. 8, p. 378-383. Also, "hsa-mir-5001" (miRBase Accession No. MI0017867, SEQ ID NO: 315) having a hairpin-like structure is known as a precursor of "hsa-miR-5001-5p".

The term "hsa-miR-1228-5p gene" or "hsa-miR-1228-5p" used herein includes the hsa-miR-1228-5p gene (miRBase Accession No. MIMAT0005582) described in SEQ ID NO: 93, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1228-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1228" (miRBase Accession No. MI0006318, SEQ ID NO: 316) having a hairpin-like structure is known as a precursor of "hsa-miR-1228-5p".

The term "hsa-miR-5572 gene" or "hsa-miR-5572" used herein includes the hsa-miR-5572 gene (miRBase Accession No. MIMAT0022260) described in SEQ ID NO: 94, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5572 gene can be obtained by a method described in Tandon M et al., 2012, Oral Dis, Vol. 18, p. 127-131. Also, "hsa-mir-5572" (miRBase Accession No. MI0019117, SEQ ID NO: 317) having a hairpin-like structure is known as a precursor of "hsa-miR-5572".

The term "hsa-miR-4327 gene" or "hsa-miR-4327" used herein includes the hsa-miR-4327 gene (miRBase Accession No. MIMAT0016889) described in SEQ ID NO: 95, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4327 gene can be obtained by a method described in Goff L A et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4327" (miRBase Accession No. MI0015867, SEQ ID NO: 318) having a hairpin-like structure is known as a precursor of "hsa-miR-4327".

The term "hsa-miR-4638-5p gene" or "hsa-miR-4638-5p" used herein includes the hsa-miR-4638-5p gene (miRBase Accession No. MIMAT0019695) described in SEQ ID NO: 96, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4638-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4638" (miRBase Accession No. MI0017265, SEQ ID NO: 319) having a hairpin-like structure is known as a precursor of "hsa-miR-4638-5p".

The term "hsa-miR-6799-5p gene" or "hsa-miR-6799-5p" used herein includes the hsa-miR-6799-5p gene (miRBase Accession No. MIMAT0027498) described in SEQ ID NO: 97, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6799-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6799" (miRBase Accession No. MI0022644, SEQ ID NO: 320) having a hairpin-like structure is known as a precursor of "hsa-miR-6799-5p".

The term "hsa-miR-6861-5p gene" or "hsa-miR-6861-5p" used herein includes the hsa-miR-6861-5p gene (miRBase Accession No. MIMAT0027623) described in SEQ ID NO: 98, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6861-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6861" (miRBase Accession No. MI0022708, SEQ ID NO: 321) having a hairpin-like structure is known as a precursor of "hsa-miR-6861-5p".

The term "hsa-miR-6727-5p gene" or "hsa-miR-6727-5p" used herein includes the hsa-miR-6727-5p gene (miRBase Accession No. MIMAT0027355) described in SEQ ID NO: 99, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6727-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6727" (miRBase Accession No. MI0022572, SEQ ID NO: 322) having a hairpin-like structure is known as a precursor of "hsa-miR-6727-5p".

The term "hsa-miR-4513 gene" or "hsa-miR-4513" used herein includes the hsa-miR-4513 gene (miRBase Accession No. MIMAT0019050) described in SEQ ID NO: 100, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4513 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4513" (miRBase Accession No. MI0016879, SEQ ID NO: 323) having a hairpin-like structure is known as a precursor of "hsa-miR-4513".

The term "hsa-miR-6805-3p gene" or "hsa-miR-6805-3p" used herein includes the hsa-miR-6805-3p gene (miRBase Accession No. MIMAT0027511) described in SEQ ID NO: 101, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6805-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6805" (miRBase Accession No. MI0022650, SEQ ID NO: 324) having a hairpin-like structure is known as a precursor of "hsa-miR-6805-3p".

The term "hsa-miR-6808-5p gene" or "hsa-miR-6808-5p" used herein includes the hsa-miR-6808-5p gene (miRBase Accession No. MIMAT0027516) described in SEQ ID NO: 102, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6808-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6808" (miRBase Accession No. MI0022653, SEQ ID NO: 325) having a hairpin-like structure is known as a precursor of "hsa-miR-6808-5p".

The term "hsa-miR-4449 gene" or "hsa-miR-4449" used herein includes the hsa-miR-4449 gene (miRBase Accession No. MIMAT0018968) described in SEQ ID NO: 103, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4449 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4449" (miRBase Accession No. MI0016792, SEQ ID NO: 326) having a hairpin-like structure is known as a precursor of "hsa-miR-4449".

The term "hsa-miR-1199-5p gene" or "hsa-miR-1199-5p" used herein includes the hsa-miR-1199-5p gene (miRBase Accession No. MIMAT0031119) described in SEQ ID NO: 104, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1199-5p gene can be obtained by a method described in Salvi A et al., 2013, Int J Oncol, Vol. 42, p. 391-402. Also, "hsa-mir-1199" (miRBase Accession No. MI0020340, SEQ ID NO: 327) having a hairpin-like structure is known as a precursor of "hsa-miR-1199-5p".

The term "hsa-miR-1275 gene" or "hsa-miR-1275" used herein includes the hsa-miR-1275 gene (miRBase Accession No. MIMAT0005929) described in SEQ ID NO: 105, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1275 gene can be obtained by a method described in Morin R D et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1275" (miRBase Accession No. MI0006415, SEQ ID NO: 328) having a hairpin-like structure is known as a precursor of "hsa-miR-1275".

The term "hsa-miR-4792 gene" or "hsa-miR-4792" used herein includes the hsa-miR-4792 gene (miRBase Accession No. MIMAT0019964) described in SEQ ID NO: 106, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4792 gene can be obtained by a

method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4792" (miRBase Accession No. MI0017439, SEQ ID NO: 329) having a hairpin-like structure is known as a precursor of "hsa-miR-4792".

The term "hsa-miR-4443 gene" or "hsa-miR-4443" used herein includes the hsa-miR-4443 gene (miRBase Accession No. MIMAT0018961) described in SEQ ID NO: 107, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4443 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4443" (miRBase Accession No. MI0016786, SEQ ID NO: 330) having a hairpin-like structure is known as a precursor of "hsa-miR-4443".

The term "hsa-miR-6891-5p gene" or "hsa-miR-6891-5p" used herein includes the hsa-miR-6891-5p gene (miRBase Accession No. MIMAT0027682) described in SEQ ID NO: 108, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6891-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6891" (miRBase Accession No. MI0022738, SEQ ID NO: 331) having a hairpin-like structure is known as a precursor of "hsa-miR-6891-5p".

The term "hsa-miR-6826-5p gene" or "hsa-miR-6826-5p" used herein includes the hsa-miR-6826-5p gene (miRBase Accession No. MIMAT0027552) described in SEQ ID NO: 109, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6826-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6826" (miRBase Accession No. MI0022671, SEQ ID NO: 332) having a hairpin-like structure is known as a precursor of "hsa-miR-6826-5p".

The term "hsa-miR-6807-5p gene" or "hsa-miR-6807-5p" used herein includes the hsa-miR-6807-5p gene (miRBase Accession No. MIMAT0027514) described in SEQ ID NO: 110, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6807-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6807" (miRBase Accession No. MI0022652, SEQ ID NO: 333) having a hairpin-like structure is known as a precursor of "hsa-miR-6807-5p".

The term "hsa-miR-7150 gene" or "hsa-miR-7150" used herein includes the hsa-miR-7150 gene (miRBase Accession No. MIMAT0028211) described in SEQ ID NO: 111, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7150 gene can be obtained by a method described in Oulas A et al., 2009, Nucleic Acids Res, Vol. 37, p. 3276-3287. Also, "hsa-mir-7150" (miRBase Accession No. MI0023610, SEQ ID NO: 334) having a hairpin-like structure is known as a precursor of "hsa-miR-7150".

The term "hsa-miR-4534 gene" or "hsa-miR-4534" used herein includes the hsa-miR-4534 gene (miRBase Accession No. MIMAT0019073) described in SEQ ID NO: 112, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4534 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4534" (miRBase Accession No. MI0016901, SEQ ID NO: 335) having a hairpin-like structure is known as a precursor of "hsa-miR-4534".

The term "hsa-miR-4476 gene" or "hsa-miR-4476" used herein includes the hsa-miR-4476 gene (miRBase Accession No. MIMAT0019003) described in SEQ ID NO: 113, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4476 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4476" (miRBase Accession No. MI0016828, SEQ ID NO: 336) having a hairpin-like structure is known as a precursor of "hsa-miR-4476".

The term "hsa-miR-4649-5p gene" or "hsa-miR-4649-5p" used herein includes the hsa-miR-4649-5p gene (miRBase Accession No. MIMAT0019711) described in SEQ ID NO: 114, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4649-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4649" (miRBase Accession No. MI0017276, SEQ ID NO: 337) having a hairpin-like structure is known as a precursor of "hsa-miR-4649-5p".

The term "hsa-miR-4525 gene" or "hsa-miR-4525" used herein includes the hsa-miR-4525 gene (miRBase Accession No. MIMAT0019064) described in SEQ ID NO: 115, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4525 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4525" (miRBase Accession No. MI0016892, SEQ ID NO: 338) having a hairpin-like structure is known as a precursor of "hsa-miR-4525".

The term "hsa-miR-1915-3p gene" or "hsa-miR-1915-3p" used herein includes the hsa-miR-1915-3p gene (miRBase Accession No. MIMAT0007892) described in SEQ ID NO: 116, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1915-3p gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1915" (miRBase Accession No. MI0008336, SEQ ID NO: 311) having a hairpin-like structure is known as a precursor of "hsa-miR-1915-3p".

The term "hsa-miR-4516 gene" or "hsa-miR-4516" used herein includes the hsa-miR-4516 gene (miRBase Accession No. MIMAT0019053) described in SEQ ID NO: 117, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4516 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4516" (miRBase Accession No. MI0016882, SEQ ID NO: 339) having a hairpin-like structure is known as a precursor of "hsa-miR-4516".

The term "hsa-miR-4417 gene" or "hsa-miR-4417" used herein includes the hsa-miR-4417 gene (miRBase Accession No. MIMAT0018929) described in SEQ ID NO: 118, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4417 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4417" (miRBase Accession No. MI0016753, SEQ ID NO: 340) having a hairpin-like structure is known as a precursor of "hsa-miR-4417".

The term "hsa-miR-642b-3p gene" or "hsa-miR-642b-3p" used herein includes the hsa-miR-642b-3p gene (miRBase Accession No. MIMAT0018444) described in SEQ ID NO: 119, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-642b-3p gene can be obtained by a method described in Witten D et al., 2010, BMC Biol, Vol. 8, p. 58. Also, "hsa-mir-642b" (miRBase Accession No. MI0016685, SEQ ID NO: 341) having a hairpin-like structure is known as a precursor of "hsa-miR-642b-3p".

The term "hsa-miR-3141 gene" or "hsa-miR-3141" used herein includes the hsa-miR-3141 gene (miRBase Accession No. MIMAT0015010) described in SEQ ID NO: 120, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3141 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol.

5, e9685. Also, "hsa-mir-3141" (miRBase Accession No. MI0014165, SEQ ID NO: 342) having a hairpin-like structure is known as a precursor of "hsa-miR-3141".

The term "hsa-miR-5100 gene" or "hsa-miR-5100" used herein includes the hsa-miR-5100 gene (miRBase Accession No. MIMAT0022259) described in SEQ ID NO: 121, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5100 gene can be obtained by a method described in Tandon M et al., 2012, Oral Dis, Vol. 18, p. 127-131. Also, "hsa-mir-5100" (miRBase Accession No. MI0019116, SEQ ID NO: 343) having a hairpin-like structure is known as a precursor of "hsa-miR-5100".

The term "hsa-miR-6848-5p gene" or "hsa-miR-6848-5p" used herein includes the hsa-miR-6848-5p gene (miRBase Accession No. MIMAT0027596) described in SEQ ID NO: 122, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6848-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6848" (miRBase Accession No. MI0022694, SEQ ID NO: 344) having a hairpin-like structure is known as a precursor of "hsa-miR-6848-5p".

The term "hsa-miR-4739 gene" or "hsa-miR-4739" used herein includes the hsa-miR-4739 gene (miRBase Accession No. MIMAT0019868) described in SEQ ID NO: 123, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4739 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4739" (miRBase Accession No. MI0017377, SEQ ID NO: 345) having a hairpin-like structure is known as a precursor of "hsa-miR-4739".

The term "hsa-miR-4459 gene" or "hsa-miR-4459" used herein includes the hsa-miR-4459 gene (miRBase Accession No. MIMAT0018981) described in SEQ ID NO: 124, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4459 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4459" (miRBase Accession No. MI0016805, SEQ ID NO: 346) having a hairpin-like structure is known as a precursor of "hsa-miR-4459".

The term "hsa-miR-1237-5p gene" or "hsa-miR-1237-5p" used herein includes the hsa-miR-1237-5p gene (miRBase Accession No. MIMAT0022946) described in SEQ ID NO: 125, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1237-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1237" (miRBase Accession No. MI0006327, SEQ ID NO: 347) having a hairpin-like structure is known as a precursor of "hsa-miR-1237-5p".

The term "hsa-miR-296-3p gene" or "hsa-miR-296-3p" used herein includes the hsa-miR-296-3p gene (miRBase Accession No. MIMAT0004679) described in SEQ ID NO: 126, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-296-3p gene can be obtained by a method described in Houbaviy H B et al., 2003, Dev Cell, Vol. 5, p. 351-358. Also, "hsa-mir-296" (miRBase Accession No. MI0000747, SEQ ID NO: 273) having a hairpin-like structure is known as a precursor of "hsa-miR-296-3p".

The term "hsa-miR-4665-3p gene" or "hsa-miR-4665-3p" used herein includes the hsa-miR-4665-3p gene (miRBase Accession No. MIMAT0019740) described in SEQ ID NO: 127, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4665-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4665" (miRBase Accession No. MI0017295, SEQ ID NO: 269) having a hairpin-like structure is known as a precursor of "hsa-miR-4665-3p".

The term "hsa-miR-6786-5p gene" or "hsa-miR-6786-5p" used herein includes the hsa-miR-6786-5p gene (miRBase Accession No. MIMAT0027472) described in SEQ ID NO: 128, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6786-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6786" (miRBase Accession No. MI0022631, SEQ ID NO: 348) having a hairpin-like structure is known as a precursor of "hsa-miR-6786-5p".

The term "hsa-miR-4258 gene" or "hsa-miR-4258" used herein includes the hsa-miR-4258 gene (miRBase Accession No. MIMAT0016879) described in SEQ ID NO: 129, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4258 gene can be obtained by a method described in Goff L A et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4258" (miRBase Accession No. MI0015857, SEQ ID NO: 349) having a hairpin-like structure is known as a precursor of "hsa-miR-4258".

The term "hsa-miR-6510-5p gene" or "hsa-miR-6510-5p" used herein includes the hsa-miR-6510-5p gene (miRBase Accession No. MIMAT0025476) described in SEQ ID NO: 130, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6510-5p gene can be obtained by a method described in Joyce C E et al., 2011, Hum Mol Genet, Vol. 20, p. 4025-4040. Also, "hsa-mir-6510" (miRBase Accession No. MI0022222, SEQ ID NO: 350) having a hairpin-like structure is known as a precursor of "hsa-miR-6510-5p".

The term "hsa-miR-1343-5p gene" or "hsa-miR-1343-5p" used herein includes the hsa-miR-1343-5p gene (miRBase Accession No. MIMAT0027038) described in SEQ ID NO: 131, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1343-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-1343" (miRBase Accession No. MI0017320, SEQ ID NO: 225) having a hairpin-like structure is known as a precursor of "hsa-miR-1343-5p".

The term "hsa-miR-1247-3p gene" or "hsa-miR-1247-3p" used herein includes the hsa-miR-1247-3p gene (miRBase Accession No. MIMAT0022721) described in SEQ ID NO: 132, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1247-3p gene can be obtained by a method described in Morin R D et al., 2008, Genome Res, Vol. 18, p. 610-621. Also, "hsa-mir-1247" (miRBase Accession No. MI0006382, SEQ ID NO: 351) having a hairpin-like structure is known as a precursor of "hsa-miR-1247-3p".

The term "hsa-miR-6805-5p gene" or "hsa-miR-6805-5p" used herein includes the hsa-miR-6805-5p gene (miRBase Accession No. MIMAT0027510) described in SEQ ID NO: 133, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6805-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6805" (miRBase Accession No. MI0022650, SEQ ID NO: 324) having a hairpin-like structure is known as a precursor of "hsa-miR-6805-5p".

The term "hsa-miR-4492 gene" or "hsa-miR-4492" used herein includes the hsa-miR-4492 gene (miRBase Accession No. MIMAT0019027) described in SEQ ID NO: 134, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4492 gene can be obtained by a

method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4492" (miRBase Accession No. MI0016854, SEQ ID NO: 352) having a hairpin-like structure is known as a precursor of "hsa-miR-4492".

The term "hsa-miR-1469 gene" or "hsa-miR-1469" used herein includes the hsa-miR-1469 gene (miRBase Accession No. MIMAT0007347) described in SEQ ID NO: 135, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1469 gene can be obtained by a method described in Kawaji H et al., 2008, BMC Genomics, Vol. 9, p. 157. Also, "hsa-mir-1469" (miRBase Accession No. MI0007074, SEQ ID NO: 353) having a hairpin-like structure is known as a precursor of "hsa-miR-1469".

The term "hsa-miR-1268b gene" or "hsa-miR-1268b" used herein includes the hsa-miR-1268b gene (miRBase Accession No. MIMAT0018925) described in SEQ ID NO: 136, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1268b gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-1268b" (miRBase Accession No. MI0016748, SEQ ID NO: 354) having a hairpin-like structure is known as a precursor of "hsa-miR-1268b".

The term "hsa-miR-6858-5p gene" or "hsa-miR-6858-5p" used herein includes the hsa-miR-6858-5p gene (miRBase Accession No. MIMAT0027616) described in SEQ ID NO: 137, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6858-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6858" (miRBase Accession No. MI0022704, SEQ ID NO: 355) having a hairpin-like structure is known as a precursor of "hsa-miR-6858-5p".

The term "hsa-miR-3937 gene" or "hsa-miR-3937" used herein includes the hsa-miR-3937 gene (miRBase Accession No. MIMAT0018352) described in SEQ ID NO: 138, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3937 gene can be obtained by a method described in Liao J Y et al., 2010, PLoS One, Vol. 5, e10563. Also, "hsa-mir-3937" (miRBase Accession No. MI0016593, SEQ ID NO: 356) having a hairpin-like structure is known as a precursor of "hsa-miR-3937".

The term "hsa-miR-939-5p gene" or "hsa-miR-939-5p" used herein includes the hsa-miR-939-5p gene (miRBase Accession No. MIMAT0004982) described in SEQ ID NO: 139, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-939-5p gene can be obtained by a method described in Lui W O et al., 2007, Cancer Res, Vol. 67, p. 6031-6043. Also, "hsa-mir-939" (miRBase Accession No. MI0005761, SEQ ID NO: 357) having a hairpin-like structure is known as a precursor of "hsa-miR-939-5p".

The term "hsa-miR-3656 gene" or "hsa-miR-3656" used herein includes the hsa-miR-3656 gene (miRBase Accession No. MIMAT0018076) described in SEQ ID NO: 140, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3656 gene can be obtained by a method described in Meiri E et al., 2010, Nucleic Acids Res, Vol. 38, p. 6234-6246. Also, "hsa-mir-3656" (miRBase Accession No. MI0016056, SEQ ID NO: 358) having a hairpin-like structure is known as a precursor of "hsa-miR-3656".

The term "hsa-miR-744-5p gene" or "hsa-miR-744-5p" used herein includes the hsa-miR-744-5p gene (miRBase Accession No. MIMAT0004945) described in SEQ ID NO: 141, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-744-5p gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-744" (miRBase Accession No. MI0005559, SEQ ID NO: 359) having a hairpin-like structure is known as a precursor of "hsa-miR-744-5p".

The term "hsa-miR-4687-3p gene" or "hsa-miR-4687-3p" used herein includes the hsa-miR-4687-3p gene (miRBase Accession No. MIMAT0019775) described in SEQ ID NO: 142, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4687-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4687" (miRBase Accession No. MI0017319, SEQ ID NO: 360) having a hairpin-like structure is known as a precursor of "hsa-miR-4687-3p".

The term "hsa-miR-4763-3p gene" or "hsa-miR-4763-3p" used herein includes the hsa-miR-4763-3p gene (miRBase Accession No. MIMAT0019913) described in SEQ ID NO: 143, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4763-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4763" (miRBase Accession No. MI0017404, SEQ ID NO: 361) having a hairpin-like structure is known as a precursor of "hsa-miR-4763-3p".

The term "hsa-miR-3620-5p gene" or "hsa-miR-3620-5p" used herein includes the hsa-miR-3620-5p gene (miRBase Accession No. MIMAT0022967) described in SEQ ID NO: 144, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3620-5p gene can be obtained by a method described in Witten D et al., 2010, BMC Biol, Vol. 8, p. 58. Also, "hsa-mir-3620" (miRBase Accession No. MI0016011, SEQ ID NO: 362) having a hairpin-like structure is known as a precursor of "hsa-miR-3620-5p".

The term "hsa-miR-3195 gene" or "hsa-miR-3195" used herein includes the hsa-miR-3195 gene (miRBase Accession No. MIMAT0015079) described in SEQ ID NO: 145, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3195 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3195" (miRBase Accession No. MI0014240, SEQ ID NO: 363) having a hairpin-like structure is known as a precursor of "hsa-miR-3195".

The term "hsa-miR-6842-5p gene" or "hsa-miR-6842-5p" used herein includes the hsa-miR-6842-5p gene (miRBase Accession No. MIMAT0027586) described in SEQ ID NO: 146, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6842-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6842" (miRBase Accession No. MI0022688, SEQ ID NO: 364) having a hairpin-like structure is known as a precursor of "hsa-miR-6842-5p".

The term "hsa-miR-4707-5p gene" or "hsa-miR-4707-5p" used herein includes the hsa-miR-4707-5p gene (miRBase Accession No. MIMAT0019807) described in SEQ ID NO: 147, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4707-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4707" (miRBase Accession No. MI0017340, SEQ ID NO: 365) having a hairpin-like structure is known as a precursor of "hsa-miR-4707-5p".

The term "hsa-miR-642a-3p gene" or "hsa-miR-642a-3p" used herein includes the hsa-miR-642a-3p gene (miRBase Accession No. MIMAT0020924) described in SEQ ID NO:

148, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-642a-3p gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-642a" (miRBase Accession No. MI0003657, SEQ ID NO: 366) having a hairpin-like structure is known as a precursor of "hsa-miR-642a-3p".

The term "hsa-miR-7113-3p gene" or "hsa-miR-7113-3p" used herein includes the hsa-miR-7113-3p gene (miRBase Accession No. MIMAT0028124) described in SEQ ID NO: 149, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7113-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7113" (miRBase Accession No. MI0022964, SEQ ID NO: 367) having a hairpin-like structure is known as a precursor of "hsa-miR-7113-3p".

The term "hsa-miR-4728-5p gene" or "hsa-miR-4728-5p" used herein includes the hsa-miR-4728-5p gene (miRBase Accession No. MIMAT0019849) described in SEQ ID NO: 150, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4728-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4728" (miRBase Accession No. MI0017365, SEQ ID NO: 368) having a hairpin-like structure is known as a precursor of "hsa-miR-4728-5p".

The term "hsa-miR-5195-3p gene" or "hsa-miR-5195-3p" used herein includes the hsa-miR-5195-3p gene (miRBase Accession No. MIMAT0021127) described in SEQ ID NO: 151, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5195-3p gene can be obtained by a method described in Schotte D et al., 2011, Leukemia, Vol. 25, p. 1389-1399. Also, "hsa-mir-5195" (miRBase Accession No. MI0018174, SEQ ID NO: 369) having a hairpin-like structure is known as a precursor of "hsa-miR-5195-3p".

The term "hsa-miR-1185-1-3p gene" or "hsa-miR-1185-1-3p" used herein includes the hsa-miR-1185-1-3p gene (miRBase Accession No. MIMAT0022838) described in SEQ ID NO: 152, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1185-1-3p gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-1185-1" (miRBase Accession No. MI0003844, SEQ ID NO: 370) having a hairpin-like structure is known as a precursor of "hsa-miR-1185-1-3p".

The term "hsa-miR-6774-5p gene" or "hsa-miR-6774-5p" used herein includes the hsa-miR-6774-5p gene (miRBase Accession No. MIMAT0027448) described in SEQ ID NO: 153, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6774-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6774" (miRBase Accession No. MI0022619, SEQ ID NO: 371) having a hairpin-like structure is known as a precursor of "hsa-miR-6774-5p".

The term "hsa-miR-8059 gene" or "hsa-miR-8059" used herein includes the hsa-miR-8059 gene (miRBase Accession No. MIMAT0030986) described in SEQ ID NO: 154, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-8059 gene can be obtained by a method described in Wang H J et al., 2013, Shock, Vol. 39, p. 480-487. Also, "hsa-mir-8059" (miRBase Accession No. MI0025895, SEQ ID NO: 372) having a hairpin-like structure is known as a precursor of "hsa-miR-8059".

The term "hsa-miR-3131 gene" or "hsa-miR-3131" used herein includes the hsa-miR-3131 gene (miRBase Accession No. MIMAT0014996) described in SEQ ID NO: 155, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3131 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3131" (miRBase Accession No. MI0014151, SEQ ID NO: 373) having a hairpin-like structure is known as a precursor of "hsa-miR-3131".

The term "hsa-miR-7847-3p gene" or "hsa-miR-7847-3p" used herein includes the hsa-miR-7847-3p gene (miRBase Accession No. MIMAT0030422) described in SEQ ID NO: 156, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7847-3p gene can be obtained by a method described in Ple H et al., 2012, PLoS One, Vol. 7, e50746. Also, "hsa-mir-7847" (miRBase Accession No. MI0025517, SEQ ID NO: 374) having a hairpin-like structure is known as a precursor of "hsa-miR-7847-3p".

The term "hsa-miR-4463 gene" or "hsa-miR-4463" used herein includes the hsa-miR-4463 gene (miRBase Accession No. MIMAT0018987) described in SEQ ID NO: 157, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4463 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4463" (miRBase Accession No. MI0016811, SEQ ID NO: 375) having a hairpin-like structure is known as a precursor of "hsa-miR-4463".

The term "hsa-miR-128-2-5p gene" or "hsa-miR-128-2-5p" used herein includes the hsa-miR-128-2-5p gene (miRBase Accession No. MIMAT0031095) described in SEQ ID NO: 158, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-128-2-5p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-128-2" (miRBase Accession No. MI0000727, SEQ ID NO: 376) having a hairpin-like structure is known as a precursor of "hsa-miR-128-2-5p".

The term "hsa-miR-4508 gene" or "hsa-miR-4508" used herein includes the hsa-miR-4508 gene (miRBase Accession No. MIMAT0019045) described in SEQ ID NO: 159, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4508 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4508" (miRBase Accession No. MI0016872, SEQ ID NO: 377) having a hairpin-like structure is known as a precursor of "hsa-miR-4508".

The term "hsa-miR-6806-5p gene" or "hsa-miR-6806-5p" used herein includes the hsa-miR-6806-5p gene (miRBase Accession No. MIMAT0027512) described in SEQ ID NO: 160, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6806-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6806" (miRBase Accession No. MI0022651, SEQ ID NO: 378) having a hairpin-like structure is known as a precursor of "hsa-miR-6806-5p".

The term "hsa-miR-7111-5p gene" or "hsa-miR-7111-5p" used herein includes the hsa-miR-7111-5p gene (miRBase Accession No. MIMAT0028119) described in SEQ ID NO: 161, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-7111-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-7111" (miRBase Accession No. MI0022962, SEQ ID NO: 379) having a hairpin-like structure is known as a precursor of "hsa-miR-7111-5p".

The term "hsa-miR-6782-5p gene" or "hsa-miR-6782-5p" used herein includes the hsa-miR-6782-5p gene (miRBase Accession No. MIMAT0027464) described in SEQ ID NO: 162, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6782-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6782" (miRBase Accession No. MI0022627, SEQ ID NO: 380) having a hairpin-like structure is known as a precursor of "hsa-miR-6782-5p".

The term "hsa-miR-4734 gene" or "hsa-miR-4734" used herein includes the hsa-miR-4734 gene (miRBase Accession No. MIMAT0019859) described in SEQ ID NO: 163, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4734 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4734" (miRBase Accession No. MI0017371, SEQ ID NO: 381) having a hairpin-like structure is known as a precursor of "hsa-miR-4734".

The term "hsa-miR-3162-5p gene" or "hsa-miR-3162-5p" used herein includes the hsa-miR-3162-5p gene (miRBase Accession No. MIMAT0015036) described in SEQ ID NO: 164, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3162-5p gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3162" (miRBase Accession No. MI0014192, SEQ ID NO: 382) having a hairpin-like structure is known as a precursor of "hsa-miR-3162-5p".

The term "hsa-miR-887-3p gene" or "hsa-miR-887-3p" used herein includes the hsa-miR-887-3p gene (miRBase Accession No. MIMAT0004951) described in SEQ ID NO: 165, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-887-3p gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-887" (miRBase Accession No. MI0005562, SEQ ID NO: 383) having a hairpin-like structure is known as a precursor of "hsa-miR-887-3p".

The term "hsa-miR-6752-5p gene" or "hsa-miR-6752-5p" used herein includes the hsa-miR-6752-5p gene (miRBase Accession No. MIMAT0027404) described in SEQ ID NO: 166, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6752-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6752" (miRBase Accession No. MI0022597, SEQ ID NO: 384) having a hairpin-like structure is known as a precursor of "hsa-miR-6752-5p".

The term "hsa-miR-6724-5p gene" or "hsa-miR-6724-5p" used herein includes the hsa-miR-6724-5p gene (miRBase Accession No. MIMAT0025856) described in SEQ ID NO: 167, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6724-5p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6724" (miRBase Accession No. MI0022559, SEQ ID NO: 385) having a hairpin-like structure is known as a precursor of "hsa-miR-6724-5p".

The term "hsa-miR-23b-3p gene" or "hsa-miR-23b-3p" used herein includes the hsa-miR-23b-3p gene (miRBase Accession No. MIMAT0000418) described in SEQ ID NO: 168, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-23b-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-23b" (miRBase Accession No. MI0000439, SEQ ID NO: 386) having a hairpin-like structure is known as a precursor of "hsa-miR-23b-3p".

The term "hsa-miR-23a-3p gene" or "hsa-miR-23a-3p" used herein includes the hsa-miR-23a-3p gene (miRBase Accession No. MIMAT0000078) described in SEQ ID NO: 169, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-23a-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2001, Science, Vol. 294, p. 853-858. Also, "hsa-mir-23a" (miRBase Accession No. MI0000079, SEQ ID NO: 387) having a hairpin-like structure is known as a precursor of "hsa-miR-23a-3p".

The term "hsa-miR-625-3p gene" or "hsa-miR-625-3p" used herein includes the hsa-miR-625-3p gene (miRBase Accession No. MIMAT0004808) described in SEQ ID NO: 170, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-625-3p gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci U.S.A., Vol. 103, p. 3687-3692. Also, "hsa-mir-625" (miRBase Accession No. MI0003639, SEQ ID NO: 388) having a hairpin-like structure is known as a precursor of "hsa-miR-625-3p".

The term "hsa-miR-1228-3p gene" or "hsa-miR-1228-3p" used herein includes the hsa-miR-1228-3p gene (miRBase Accession No. MIMAT0005583) described in SEQ ID NO: 171, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1228-3p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1228" (miRBase Accession No. MI0006318, SEQ ID NO: 316) having a hairpin-like structure is known as a precursor of "hsa-miR-1228-3p".

The term "hsa-miR-614 gene" or "hsa-miR-614" used herein includes the hsa-miR-614 gene (miRBase Accession No. MIMAT0003282) described in SEQ ID NO: 172, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-614 gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-614" (miRBase Accession No. MI0003627, SEQ ID NO: 389) having a hairpin-like structure is known as a precursor of "hsa-miR-614".

The term "hsa-miR-1913 gene" or "hsa-miR-1913" used herein includes the hsa-miR-1913 gene (miRBase Accession No. MIMAT0007888) described in SEQ ID NO: 173, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1913 gene can be obtained by a method described in Bar M et al., 2008, Stem Cells, Vol. 26, p. 2496-2505. Also, "hsa-mir-1913" (miRBase Accession No. MI0008334, SEQ ID NO: 390) having a hairpin-like structure is known as a precursor of "hsa-miR-1913".

The term "hsa-miR-92a-2-5p gene" or "hsa-miR-92a-2-5p" used herein includes the hsa-miR-92a-2-5p gene (miRBase Accession No. MIMAT0004508) described in SEQ ID NO: 174, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-92a-2-5p gene can be obtained by a method described in Mourelatos Z et al., 2002, Genes Dev, Vol. 16, p. 720-728. Also, "hsa-mir-92a-2" (miRBase Accession No. MI0000094, SEQ ID NO: 391) having a hairpin-like structure is known as a precursor of "hsa-miR-92a-2-5p".

The term "hsa-miR-187-5p gene" or "hsa-miR-187-5p" used herein includes the hsa-miR-187-5p gene (miRBase Accession No. MIMAT0004561) described in SEQ ID NO: 175, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-187-5p gene can be

obtained by a method described in Lim L P et al., 2003, Science, Vol. 299, p. 1540. Also, "hsa-mir-187" (miRBase Accession No. MI0000274, SEQ ID NO: 392) having a hairpin-like structure is known as a precursor of "hsa-miR-187-5p".

The term "hsa-miR-16-5p gene" or "hsa-miR-16-5p" used herein includes the hsa-miR-16-5p gene (miRBase Accession No. MIMAT0000069) described in SEQ ID NO: 176, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-16-5p gene can be obtained by a method described in Lagos-Quintana M et al., 2001, Science, Vol. 294, p. 853-858. Also, "hsa-mir-16-1" and "hsa-mir-16-2" (miRBase Accession Nos. MI0000070 and MI0000115, SEQ ID NOs: 393 and 394) having a hairpin-like structure are known as precursors of "hsa-miR-16-5p".

The term "hsa-miR-92b-3p gene" or "hsa-miR-92b-3p" used herein includes the hsa-miR-92b-3p gene (miRBase Accession No. MIMAT0003218) described in SEQ ID NO: 177, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-92b-3p gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-92b" (miRBase Accession No. MI0003560, SEQ ID NO: 395) having a hairpin-like structure is known as a precursor of "hsa-miR-92b-3p".

The term "hsa-miR-150-3p gene" or "hsa-miR-150-3p" used herein includes the hsa-miR-150-3p gene (miRBase Accession No. MIMAT0004610) described in SEQ ID NO: 178, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-150-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-150" (miRBase Accession No. MI0000479, SEQ ID NO: 396) having a hairpin-like structure is known as a precursor of "hsa-miR-150-3p".

The term "hsa-miR-564 gene" or "hsa-miR-564" used herein includes the hsa-miR-564 gene (miRBase Accession No. MIMAT0003228) described in SEQ ID NO: 179, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-564 gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-564" (miRBase Accession No. MI0003570, SEQ ID NO: 397) having a hairpin-like structure is known as a precursor of "hsa-miR-564".

The term "hsa-miR-125a-3p gene" or "hsa-miR-125a-3p" used herein includes the hsa-miR-125a-3p gene (miRBase Accession No. MIMAT0004602) described in SEQ ID NO: 180, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-125a-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-125a" (miRBase Accession No. MI0000469, SEQ ID NO: 398) having a hairpin-like structure is known as a precursor of "hsa-miR-125a-3p".

The term "hsa-miR-92b-5p gene" or "hsa-miR-92b-5p" used herein includes the hsa-miR-92b-5p gene (miRBase Accession No. MIMAT0004792) described in SEQ ID NO: 181, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-92b-5p gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-92b" (miRBase Accession No. MI0003560, SEQ ID NO: 395) having a hairpin-like structure is known as a precursor of "hsa-miR-92b-5p".

The term "hsa-miR-92a-3p gene" or "hsa-miR-92a-3p" used herein includes the hsa-miR-92a-3p gene (miRBase Accession No. MIMAT0000092) described in SEQ ID NO: 182, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-92a-3p gene can be obtained by a method described in Mourelatos Z et al., 2002, Genes Dev, Vol. 16, p. 720-728. Also, "hsa-mir-92a-1" and "hsa-mir-92a-2" (miRBase Accession Nos. MI0000093 and MI0000094, SEQ ID NOs: 399 and 391) having a hairpin-like structure are known as precursors of "hsa-miR-92a-3p".

The term "hsa-miR-663a gene" or "hsa-miR-663a" used herein includes the hsa-miR-663a gene (miRBase Accession No. MIMAT0003326) described in SEQ ID NO: 183, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-663a gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-663a" (miRBase Accession No. MI0003672, SEQ ID NO: 400) having a hairpin-like structure is known as a precursor of "hsa-miR-663a".

The term "hsa-miR-4688 gene" or "hsa-miR-4688" used herein includes the hsa-miR-4688 gene (miRBase Accession No. MIMAT0019777) described in SEQ ID NO: 184, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4688 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4688" (miRBase Accession No. MI0017321, SEQ ID NO: 401) having a hairpin-like structure is known as a precursor of "hsa-miR-4688".

The term "hsa-miR-4648 gene" or "hsa-miR-4648" used herein includes the hsa-miR-4648 gene (miRBase Accession No. MIMAT0019710) described in SEQ ID NO: 185, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4648 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4648" (miRBase Accession No. MI0017275, SEQ ID NO: 402) having a hairpin-like structure is known as a precursor of "hsa-miR-4648".

The term "hsa-miR-6085 gene" or "hsa-miR-6085" used herein includes the hsa-miR-6085 gene (miRBase Accession No. MIMAT0023710) described in SEQ ID NO: 186, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6085 gene can be obtained by a method described in Voellenkle C et al., 2012, RNA, Vol. 18, p. 472-484. Also, "hsa-mir-6085" (miRBase Accession No. MI0020362, SEQ ID NO: 403) having a hairpin-like structure is known as a precursor of "hsa-miR-6085".

The term "hsa-miR-6126 gene" or "hsa-miR-6126" used herein includes the hsa-miR-6126 gene (miRBase Accession No. MIMAT0024599) described in SEQ ID NO: 187, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6126 gene can be obtained by a method described in Smith J L et al., 2012, J Virol, Vol. 86, p. 5278-5287. Also, "hsa-mir-6126" (miRBase Accession No. MI0021260, SEQ ID NO: 404) having a hairpin-like structure is known as a precursor of "hsa-miR-6126".

The term "hsa-miR-6880-5p gene" or "hsa-miR-6880-5p" used herein includes the hsa-miR-6880-5p gene (miRBase Accession No. MIMAT0027660) described in SEQ ID NO: 188, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6880-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6880" (miRBase Accession No. MI0022727, SEQ ID NO: 405) having a hairpin-like structure is known as a precursor of "hsa-miR-6880-5p".

The term "hsa-miR-328-5p gene" or "hsa-miR-328-5p" used herein includes the hsa-miR-328-5p gene (miRBase Accession No. MIMAT0026486) described in SEQ ID NO: 189, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-328-5p gene can be obtained by a method described in Kim J et al., 2004, Proc Natl Acad Sci USA, Vol. 101, p. 360-365. Also, "hsa-mir-328" (miRBase Accession No. MI0000804, SEQ ID NO: 406) having a hairpin-like structure is known as a precursor of "hsa-miR-328-5p".

The term "hsa-miR-6768-5p gene" or "hsa-miR-6768-5p" used herein includes the hsa-miR-6768-5p gene (miRBase Accession No. MIMAT0027436) described in SEQ ID NO: 190, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6768-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6768" (miRBase Accession No. MI0022613, SEQ ID NO: 407) having a hairpin-like structure is known as a precursor of "hsa-miR-6768-5p".

The term "hsa-miR-3180 gene" or "hsa-miR-3180" used herein includes the hsa-miR-3180 gene (miRBase Accession No. MIMAT0018178) described in SEQ ID NO: 191, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3180 gene can be obtained by a method described in Creighton C J et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3180-4" and "hsa-mir-3180-5" (miRBase Accession Nos. MI0016408 and MI0016409, SEQ ID NOs: 408 and 409) having a hairpin-like structure are known as precursors of "hsa-miR-3180".

The term "hsa-miR-6087 gene" or "hsa-miR-6087" used herein includes the hsa-miR-6087 gene (miRBase Accession No. MIMAT0023712) described in SEQ ID NO: 192, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6087 gene can be obtained by a method described in Yoo J K et al., 2012, Stem Cells Dev, Vol. 21, p. 2049-2057. Also, "hsa-mir-6087" (miRBase Accession No. MI0020364, SEQ ID NO: 410) having a hairpin-like structure is known as a precursor of "hsa-miR-6087".

The term "hsa-miR-1273g-3p gene" or "hsa-miR-1273g-3p" used herein includes the hsa-miR-1273g-3p gene (miRBase Accession No. MIMAT0022742) described in SEQ ID NO: 193, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1273g-3p gene can be obtained by a method described in Reshmi G et al., 2011, Genomics, Vol. 97, p. 333-340. Also, "hsa-mir-1273g" (miRBase Accession No. MI0018003, SEQ ID NO: 411) having a hairpin-like structure is known as a precursor of "hsa-miR-1273g-3p".

The term "hsa-miR-1225-5p gene" or "hsa-miR-1225-5p" used herein includes the hsa-miR-1225-5p gene (miRBase Accession No. MIMAT0005572) described in SEQ ID NO: 194, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1225-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1225" (miRBase Accession No. MI0006311, SEQ ID NO: 303) having a hairpin-like structure is known as a precursor of "hsa-miR-1225-5p".

The term "hsa-miR-3196 gene" or "hsa-miR-3196" used herein includes the hsa-miR-3196 gene (miRBase Accession No. MIMAT0015080) described in SEQ ID NO: 195, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3196 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3196" (miRBase Accession No. MI0014241, SEQ ID NO: 412) having a hairpin-like structure is known as a precursor of "hsa-miR-3196".

The term "hsa-miR-4695-5p gene" or "hsa-miR-4695-5p" used herein includes the hsa-miR-4695-5p gene (miRBase Accession No. MIMAT0019788) described in SEQ ID NO: 196, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4695-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4695" (miRBase Accession No. MI0017328, SEQ ID NO: 413) having a hairpin-like structure is known as a precursor of "hsa-miR-4695-5p".

The term "hsa-miR-6732-5p gene" or "hsa-miR-6732-5p" used herein includes the hsa-miR-6732-5p gene (miRBase Accession No. MIMAT0027365) described in SEQ ID NO: 197, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6732-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6732" (miRBase Accession No. MI0022577, SEQ ID NO: 414) having a hairpin-like structure is known as a precursor of "hsa-miR-6732-5p".

The term "hsa-miR-638 gene" or "hsa-miR-638" used herein includes the hsa-miR-638 gene (miRBase Accession No. MIMAT0003308) described in SEQ ID NO: 198, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-638 gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-638" (miRBase Accession No. MI0003653, SEQ ID NO: 415) having a hairpin-like structure is known as a precursor of "hsa-miR-638".

The term "hsa-miR-6813-5p gene" or "hsa-miR-6813-5p" used herein includes the hsa-miR-6813-5p gene (miRBase Accession No. MIMAT0027526) described in SEQ ID NO: 199, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6813-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6813" (miRBase Accession No. MI0022658, SEQ ID NO: 416) having a hairpin-like structure is known as a precursor of "hsa-miR-6813-5p".

The term "hsa-miR-665 gene" or "hsa-miR-665" used herein includes the hsa-miR-665 gene (miRBase Accession No. MIMAT0004952) described in SEQ ID NO: 200, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-665 gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-665" (miRBase Accession No. MI0005563, SEQ ID NO: 417) having a hairpin-like structure is known as a precursor of "hsa-miR-665".

The term "hsa-miR-486-3p gene" or "hsa-miR-486-3p" used herein includes the hsa-miR-486-3p gene (miRBase Accession No. MIMAT0004762) described in SEQ ID NO: 201, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-486-3p gene can be obtained by a method described in Fu H et al., 2005, FEBS Lett, Vol. 579, p. 3849-3854. Also, "hsa-mir-486" and "hsa-mir-486-2" (miRBase Accession Nos. MI0002470 and MI0023622, SEQ ID NOs: 418 and 419) having a hairpin-like structure are known as precursors of "hsa-miR-486-3p".

The term "hsa-miR-4466 gene" or "hsa-miR-4466" used herein includes the hsa-miR-4466 gene (miRBase Accession No. MIMAT0018993) described in SEQ ID NO: 202, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4466 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116,

e118-e127. Also, "hsa-mir-4466" (miRBase Accession No. MI0016817, SEQ ID NO: 420) having a hairpin-like structure is known as a precursor of "hsa-miR-4466".

The term "hsa-miR-30c-1-3p gene" or "hsa-miR-30c-1-3p" used herein includes the hsa-miR-30c-1-3p gene (miRBase Accession No. MIMAT0004674) described in SEQ ID NO: 203, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-30c-1-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2002, Curr Biol, Vol. 12, p. 735-739. Also, "hsa-mir-30c-1" (miRBase Accession No. MI0000736, SEQ ID NO: 421) having a hairpin-like structure is known as a precursor of "hsa-miR-30c-1-3p".

The term "hsa-miR-3621 gene" or "hsa-miR-3621" used herein includes the hsa-miR-3621 gene (miRBase Accession No. MIMAT0018002) described in SEQ ID NO: 204, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3621 gene can be obtained by a method described in Witten D et al., 2010, BMC Biol, Vol. 8, p. 58. Also, "hsa-mir-3621" (miRBase Accession No. MI0016012, SEQ ID NO: 422) having a hairpin-like structure is known as a precursor of "hsa-miR-3621".

The term "hsa-miR-6743-5p gene" or "hsa-miR-6743-5p" used herein includes the hsa-miR-6743-5p gene (miRBase Accession No. MIMAT0027387) described in SEQ ID NO: 205, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6743-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6743" (miRBase Accession No. MI0022588, SEQ ID NO: 423) having a hairpin-like structure is known as a precursor of "hsa-miR-6743-5p".

The term "hsa-miR-4298 gene" or "hsa-miR-4298" used herein includes the hsa-miR-4298 gene (miRBase Accession No. MIMAT0016852) described in SEQ ID NO: 206, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4298 gene can be obtained by a method described in Goff L A et al., 2009, PLoS One, Vol. 4, e7192. Also, "hsa-mir-4298" (miRBase Accession No. MI0015830, SEQ ID NO: 424) having a hairpin-like structure is known as a precursor of "hsa-miR-4298".

The term "hsa-miR-4741 gene" or "hsa-miR-4741" used herein includes the hsa-miR-4741 gene (miRBase Accession No. MIMAT0019871) described in SEQ ID NO: 207, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4741 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4741" (miRBase Accession No. MI0017379, SEQ ID NO: 425) having a hairpin-like structure is known as a precursor of "hsa-miR-4741".

The term "hsa-miR-3619-3p gene" or "hsa-miR-3619-3p" used herein includes the hsa-miR-3619-3p gene (miRBase Accession No. MIMAT0019219) described in SEQ ID NO: 208, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3619-3p gene can be obtained by a method described in Witten D et al., 2010, BMC Biol, Vol. 8, p. 58. Also, "hsa-mir-3619" (miRBase Accession No. MI0016009, SEQ ID NO: 426) having a hairpin-like structure is known as a precursor of "hsa-miR-3619-3p".

The term "hsa-miR-6824-5p gene" or "hsa-miR-6824-5p" used herein includes the hsa-miR-6824-5p gene (miRBase Accession No. MIMAT0027548) described in SEQ ID NO: 209, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6824-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6824" (miRBase Accession No. MI0022669, SEQ ID NO: 427) having a hairpin-like structure is known as a precursor of "hsa-miR-6824-5p".

The term "hsa-miR-5698 gene" or "hsa-miR-5698" used herein includes the hsa-miR-5698 gene (miRBase Accession No. MIMAT0022491) described in SEQ ID NO: 210, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-5698 gene can be obtained by a method described in Watahiki A et al., 2011, PLoS One, Vol. 6, e24950. Also, "hsa-mir-5698" (miRBase Accession No. MI0019305, SEQ ID NO: 428) having a hairpin-like structure is known as a precursor of "hsa-miR-5698".

The term "hsa-miR-371a-5p gene" or "hsa-miR-371a-5p" used herein includes the hsa-miR-371a-5p gene (miRBase Accession No. MIMAT0004687) described in SEQ ID NO: 211, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-371a-5p gene can be obtained by a method described in Suh M R et al., 2004, Dev Biol, Vol. 270, p. 488-498. Also, "hsa-mir-371a" (miRBase Accession No. MI0000779, SEQ ID NO: 429) having a hairpin-like structure is known as a precursor of "hsa-miR-371a-5p".

The term "hsa-miR-4488 gene" or "hsa-miR-4488" used herein includes the hsa-miR-4488 gene (miRBase Accession No. MIMAT0019022) described in SEQ ID NO: 212, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4488 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4488" (miRBase Accession No. MI0016849, SEQ ID NO: 430) having a hairpin-like structure is known as a precursor of "hsa-miR-4488".

The term "hsa-miR-1233-5p gene" or "hsa-miR-1233-5p" used herein includes the hsa-miR-1233-5p gene (miRBase Accession No. MIMAT0022943) described in SEQ ID NO: 213, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-1233-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1233-1" and "hsa-mir-1233-2" (miRBase Accession Nos. MI0006323 and MI0015973, SEQ ID NOs: 431 and 432) having a hairpin-like structure are known as precursors of "hsa-miR-1233-5p".

The term "hsa-miR-4723-5p gene" or "hsa-miR-4723-5p" used herein includes the hsa-miR-4723-5p gene (miRBase Accession No. MIMAT0019838) described in SEQ ID NO: 214, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4723-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4723" (miRBase Accession No. MI0017359, SEQ ID NO: 433) having a hairpin-like structure is known as a precursor of "hsa-miR-4723-5p".

The term "hsa-miR-24-3p gene" or "hsa-miR-24-3p" used herein includes the hsa-miR-24-3p gene (miRBase Accession No. MIMAT0000080) described in SEQ ID NO: 215, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-24-3p gene can be obtained by a method described in Lagos-Quintana M et al., 2001, Science, Vol. 294, p. 853-858. Also, "hsa-mir-24-1" and "hsa-mir-24-2" (miRBase Accession Nos. MI0000080 and MI0000081, SEQ ID NOs: 434 and 435) having a hairpin-like structure are known as precursors of "hsa-miR-24-3p".

The term "hsa-miR-1238-5p gene" or "hsa-miR-1238-5p" used herein includes the hsa-miR-1238-5p gene (miRBase Accession No. MIMAT0022947) described in SEQ ID NO: 216, a homolog or an ortholog of a different organism

species, and the like. The hsa-miR-1238-5p gene can be obtained by a method described in Berezikov E et al., 2007, Mol Cell, Vol. 28, p. 328-336. Also, "hsa-mir-1238" (miRBase Accession No. MI0006328, SEQ ID NO: 436) having a hairpin-like structure is known as a precursor of "hsa-miR-1238-5p".

The term "hsa-miR-4442 gene" or "hsa-miR-4442" used herein includes the hsa-miR-4442 gene (miRBase Accession No. MIMAT0018960) described in SEQ ID NO: 217, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4442 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4442" (miRBase Accession No. MI0016785, SEQ ID NO: 437) having a hairpin-like structure is known as a precursor of "hsa-miR-4442".

The term "hsa-miR-3928-3p gene" or "hsa-miR-3928-3p" used herein includes the hsa-miR-3928-3p gene (miRBase Accession No. MIMAT0018205) described in SEQ ID NO: 218, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3928-3p gene can be obtained by a method described in Creighton C J et al., 2010, PLoS One, Vol. 5, e9637. Also, "hsa-mir-3928" (miRBase Accession No. MI0016438, SEQ ID NO: 438) having a hairpin-like structure is known as a precursor of "hsa-miR-3928-3p".

The term "hsa-miR-6716-5p gene" or "hsa-miR-6716-5p" used herein includes the hsa-miR-6716-5p gene (miRBase Accession No. MIMAT0025844) described in SEQ ID NO: 219, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6716-5p gene can be obtained by a method described in Li Y et al., 2012, Gene, Vol. 497, p. 330-335. Also, "hsa-mir-6716" (miRBase Accession No. MI0022550, SEQ ID NO: 439) having a hairpin-like structure is known as a precursor of "hsa-miR-6716-5p".

The term "hsa-miR-6089 gene" or "hsa-miR-6089" used herein includes the hsa-miR-6089 gene (miRBase Accession No. MIMAT0023714) described in SEQ ID NO: 220, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6089 gene can be obtained by a method described in Yoo J K et al., 2012, Stem Cells Dev, Vol. 21, p. 2049-2057. Also, "hsa-mir-6089-1" and "hsa-mir-6089-2" (miRBase Accession Nos. MI0020366 and MI0023563, SEQ ID NOs: 440 and 441) having a hairpin-like structure are known as precursors of "hsa-miR-6089".

The term "hsa-miR-6124 gene" or "hsa-miR-6124" used herein includes the hsa-miR-6124 gene (miRBase Accession No. MIMAT0024597) described in SEQ ID NO: 221, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6124 gene can be obtained by a method described in Smith J L et al., 2012, J Virol, Vol. 86, p. 5278-5287. Also, "hsa-mir-6124" (miRBase Accession No. MI0021258, SEQ ID NO: 442) having a hairpin-like structure is known as a precursor of "hsa-miR-6124".

The term "hsa-miR-6778-5p gene" or "hsa-miR-6778-5p" used herein includes the hsa-miR-6778-5p gene (miRBase Accession No. MIMAT0027456) described in SEQ ID NO: 222, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6778-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6778" (miRBase Accession No. MI0022623, SEQ ID NO: 443) having a hairpin-like structure is known as a precursor of "hsa-miR-6778-5p".

The term "hsa-miR-557 gene" or "hsa-miR-557" used herein includes the hsa-miR-557 gene (miRBase Accession No. MIMAT0003221) described in SEQ ID NO: 223, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-557 gene can be obtained by a method described in Cummins J M et al., 2006, Proc Natl Acad Sci USA, Vol. 103, p. 3687-3692. Also, "hsa-mir-557" (miRBase Accession No. MI0003563, SEQ ID NO: 444) having a hairpin-like structure is known as a precursor of "hsa-miR-557".

The term "hsa-miR-6090 gene" or "hsa-miR-6090" used herein includes the hsa-miR-6090 gene (miRBase Accession No. MIMAT0023715) described in SEQ ID NO: 224, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6090 gene can be obtained by a method described in Yoo J K et al., 2012, Stem Cells Dev, Vol. 21, p. 2049-2057. Also, "hsa-mir-6090" (miRBase Accession No. MI0020367, SEQ ID NO: 445) having a hairpin-like structure is known as a precursor of "hsa-miR-6090".

The term "hsa-miR-6757-5p gene" or "hsa-miR-6757-5p" used herein includes the hsa-miR-6757-5p gene (miRBase Accession No. MIMAT0027414) described in SEQ ID NO: 714, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6757-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6757" (miRBase Accession No. MI0022602, SEQ ID NO: 730) having a hairpin-like structure is known as a precursor of "hsa-miR-6757-5p".

The term "hsa-miR-4448 gene" or "hsa-miR-4448" used herein includes the hsa-miR-4448 gene (miRBase Accession No. MIMAT0018967) described in SEQ ID NO: 715, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4448 gene can be obtained by a method described in Jima D D et al., 2010, Blood, Vol. 116, e118-e127. Also, "hsa-mir-4448" (miRBase Accession No. MI0016791, SEQ ID NO: 731) having a hairpin-like structure is known as a precursor of "hsa-miR-4448".

The term "hsa-miR-671-5p gene" or "hsa-miR-671-5p" used herein includes the hsa-miR-671-5p gene (miRBase Accession No. MIMAT0003880) described in SEQ ID NO: 716, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-671-5p gene can be obtained by a method described in Berezikov E et al., 2006, Genome Res, Vol. 16, p. 1289-1298. Also, "hsa-mir-671" (miRBase Accession No. MI0003760, SEQ ID NO: 732) having a hairpin-like structure is known as a precursor of "hsa-miR-671-5p".

The term "hsa-miR-3178 gene" or "hsa-miR-3178" used herein includes the hsa-miR-3178 gene (miRBase Accession No. MIMAT0015055) described in SEQ ID NO: 717, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3178 gene can be obtained by a method described in Stark M S et al., 2010, PLoS One, Vol. 5, e9685. Also, "hsa-mir-3178" (miRBase Accession No. MI0014212, SEQ ID NO: 733) having a hairpin-like structure is known as a precursor of "hsa-miR-3178".

The term "hsa-miR-4725-3p gene" or "hsa-miR-4725-3p" used herein includes the hsa-miR-4725-3p gene (miRBase Accession No. MIMAT0019844) described in SEQ ID NO: 718, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4725-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4725" (miRBase Accession No. MI0017362, SEQ ID NO: 734) having a hairpin-like structure is known as a precursor of "hsa-miR-4725-3p".

The term "hsa-miR-940 gene" or "hsa-miR-940" used herein includes the hsa-miR-940 gene (miRBase Accession

No. MIMAT0004983) described in SEQ ID NO: 719, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-940 gene can be obtained by a method described in Lui W O et al., 2007, A Cancer Res., Vol. 67, p. 6031-6043. Also, "hsa-mir-940" (miRBase Accession No. MI0005762, SEQ ID NO: 735) having a hairpin-like structure is known as a precursor of "hsa-miR-940".

The term "hsa-miR-6789-5p gene" or "hsa-miR-6789-5p" used herein includes the hsa-miR-6789-5p gene (miRBase Accession No. MIMAT0027478) described in SEQ ID NO: 720, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6789-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6789" (miRBase Accession No. MI0022634, SEQ ID NO: 736) having a hairpin-like structure is known as a precursor of "hsa-miR-6789-5p".

The term "hsa-miR-4484 gene" or "hsa-miR-4484" used herein includes the hsa-miR-4484 gene (miRBase Accession No. MIMAT0019018) described in SEQ ID NO: 721, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4484 gene can be obtained by a method described in Jima D D et al., 2010, Blood., Vol. 116, e118-e127. Also, "hsa-mir-4484" (miRBase Accession No. MI0016845, SEQ ID NO: 737) having a hairpin-like structure is known as a precursor of "hsa-miR-4484".

The term "hsa-miR-4634 gene" or "hsa-miR-4634" used herein includes the hsa-miR-4634 gene (miRBase Accession No. MIMAT0019691) described in SEQ ID NO: 722, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4634 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res., Vol. 71, p. 78-86. Also, "hsa-mir-4634" (miRBase Accession No. MI0017261, SEQ ID NO: 738) having a hairpin-like structure is known as a precursor of "hsa-miR-4634".

The term "hsa-miR-4745-5p gene" or "hsa-miR-4745-5p" used herein includes the hsa-miR-4745-5p gene (miRBase Accession No. MIMAT0019878) described in SEQ ID NO: 723, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4745-5p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4745" (miRBase Accession No. MI0017384, SEQ ID NO: 739) having a hairpin-like structure is known as a precursor of "hsa-miR-4745-5p".

The term "hsa-miR-4730 gene" or "hsa-miR-4730" used herein includes the hsa-miR-4730 gene (miRBase Accession No. MIMAT0019852) described in SEQ ID NO: 724, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4730 gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4730" (miRBase Accession No. MI0017367, SEQ ID NO: 740) having a hairpin-like structure is known as a precursor of "hsa-miR-4730".

The term "hsa-miR-6803-5p gene" or "hsa-miR-6803-5p" used herein includes the hsa-miR-6803-5p gene (miRBase Accession No. MIMAT0027506) described in SEQ ID NO: 725, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6803-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6803" (miRBase Accession No. MI0022648, SEQ ID NO: 741) having a hairpin-like structure is known as a precursor of "hsa-miR-6803-5p".

The term "hsa-miR-6798-5p gene" or "hsa-miR-6798-5p" used herein includes the hsa-miR-6798-5p gene (miRBase Accession No. MIMAT0027496) described in SEQ ID NO: 726, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6798-5p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res, Vol. 22, p. 1634-1645. Also, "hsa-mir-6798" (miRBase Accession No. MI0022643, SEQ ID NO: 742) having a hairpin-like structure is known as a precursor of "hsa-miR-6798-5p".

The term "hsa-miR-3648 gene" or "hsa-miR-3648" used herein includes the hsa-miR-3648 gene (miRBase Accession No. MIMAT0018068) described in SEQ ID NO: 727, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-3648 gene can be obtained by a method described in Meiri E et al., 2010, Nucleic Acids Res, Vol. 38, p. 6234-6246. Also, "hsa-mir-3648" (miRBase Accession No. MI0016048, SEQ ID NO: 743) having a hairpin-like structure is known as a precursor of "hsa-miR-3648".

The term "hsa-miR-4783-3p gene" or "hsa-miR-4783-3p" used herein includes the hsa-miR-4783-3p gene (miRBase Accession No. MIMAT0019947) described in SEQ ID NO: 728, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-4783-3p gene can be obtained by a method described in Persson H et al., 2011, Cancer Res, Vol. 71, p. 78-86. Also, "hsa-mir-4783" (miRBase Accession No. MI0017428, SEQ ID NO: 744) having a hairpin-like structure is known as a precursor of "hsa-miR-4783-3p".

The term "hsa-miR-6836-3p gene" or "hsa-miR-6836-3p" used herein includes the hsa-miR-6836-3p gene (miRBase Accession No. MIMAT0027575) described in SEQ ID NO: 729, a homolog or an ortholog of a different organism species, and the like. The hsa-miR-6836-3p gene can be obtained by a method described in Ladewig E et al., 2012, Genome Res., Vol. 22, p. 1634-1645. Also, "hsa-mir-6836" (miRBase Accession No. MI0022682, SEQ ID NO: 745) having a hairpin-like structure is known as a precursor of "hsa-miR-6836-3p".

A mature miRNA may become a variant due to the sequence cleaved shorter or longer by one to several flanking nucleotides, or nucleotide substitution, when cleaved as the mature miRNA from its RNA precursor having a hairpin-like structure. This variant is called isomiR (Morin R D. et al., 2008, Genome Res., Vol. 18, p. 610-621). miRBase Release 20 shows the nucleotide sequences represented by SEQ ID NOs: 1 to 224 and 714 to 729 as well as a large number of the nucleotide sequence variants and fragments represented by SEQ ID NOs: 446 to 713 and 746 to 765, called isomiRs. These variants can also be obtained as miRNAs having a nucleotide sequence represented by any of SEQ ID NOs: 1 to 224 and 714 to 729.

Specifically, among the variants of polynucleotides consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1, 3, 4, 6, 7, 10, 11, 13, 14, 16, 17, 20, 22, 26, 29, 36, 38, 39, 40, 42, 43, 44, 46, 49, 52, 59, 60, 62, 63, 65, 66, 67, 72, 76, 77, 78, 81, 83, 84, 85, 86, 87, 88, 89, 90, 92, 93, 94, 96, 100, 103, 105, 106, 107, 113, 114, 115, 116, 117, 118, 119, 120, 121, 123, 124, 125, 126, 130, 132, 134, 136, 139, 140, 141, 142, 143, 144, 145, 147, 148, 150, 151, 152, 155, 157, 158, 159, 163, 164, 165, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 187, 189, 191, 192, 193, 195, 196, 198, 200, 201, 202, 203, 206, 207, 210, 211, 212, 213, 214, 215, 217, 218, 219, 220, 221, 715, 716, 717, 718, 719, 721, 723, 724, 727 and 728 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t according to the present invention, examples of the longest variants registered in miRBase Release 20 include polynucleotides rep-

resented by SEQ ID NOs: 446, 448, 450, 452, 454, 456, 458, 460, 462, 464, 466, 468, 470, 472, 474, 476, 478, 480, 482, 484, 486, 488, 490, 492, 494, 496, 498, 500, 502, 504, 506, 508, 510, 512, 514, 516, 518, 520, 522, 524, 526, 528, 530, 532, 534, 536, 538, 540, 542, 544, 546, 548, 550, 552, 554, 556, 558, 560, 562, 564, 566, 568, 570, 572, 574, 576, 578, 580, 582, 584, 586, 588, 590, 592, 594, 596, 598, 600, 602, 604, 606, 608, 610, 612, 614, 616, 618, 620, 622, 624, 626, 628, 630, 632, 634, 636, 638, 640, 642, 644, 646, 648, 650, 652, 654, 656, 658, 660, 662, 664, 666, 668, 670, 672, 674, 676, 678, 680, 682, 684, 686, 688, 690, 692, 694, 696, 698, 700, 702, 704, 706, 708, 710, 712, 746, 748, 750, 752, 754, 756, 758, 760, 762 and 764, respectively.

Also, among the variants of polynucleotides consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1, 3, 4, 6, 7, 10, 11, 13, 14, 16, 17, 20, 22, 26, 29, 36, 38, 39, 40, 42, 43, 44, 46, 49, 52, 59, 60, 62, 63, 65, 66, 67, 72, 76, 77, 78, 81, 83, 84, 85, 86, 87, 88, 89, 90, 92, 93, 94, 96, 100, 103, 105, 106, 107, 113, 114, 115, 116, 117, 118, 119, 120, 121, 123, 124, 125, 126, 130, 132, 134, 136, 139, 140, 141, 142, 143, 144, 145, 147, 148, 150, 151, 152, 155, 157, 158, 159, 163, 164, 165, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 187, 189, 191, 192, 193, 195, 196, 198, 200, 201, 202, 203, 206, 207, 210, 211, 212, 213, 214, 215, 217, 218, 219, 220, 221, 715, 716, 717, 718, 719, 721, 723, 724, 727 and 728 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t according to the present invention, examples of the shortest variants registered in miRBase Release 20 include polynucleotides having sequences represented by SEQ ID NOs: 447, 449, 451, 453, 455, 457, 459, 461, 463, 465, 467, 469, 471, 473, 475, 477, 479, 481, 483, 485, 487, 489, 491, 493, 495, 497, 499, 501, 503, 505, 507, 509, 511, 513, 515, 517, 519, 521, 523, 525, 527, 529, 531, 533, 535, 537, 539, 541, 543, 545, 547, 549, 551, 553, 555, 557, 559, 561, 563, 565, 567, 569, 571, 573, 575, 577, 579, 581, 583, 585, 587, 589, 591, 593, 595, 597, 599, 601, 603, 605, 607, 609, 611, 613, 615, 617, 619, 621, 623, 625, 627, 629, 631, 633, 635, 637, 639, 641, 643, 645, 647, 649, 651, 653, 655, 657, 659, 661, 663, 665, 667, 669, 671, 673, 675, 677, 679, 681, 683, 685, 687, 689, 691, 693, 695, 697, 699, 701, 703, 705, 707, 709, 711, 713, 747, 749, 751, 753, 755, 757, 759, 761, 763 and 765, respectively.

In addition to these variants and fragments, examples thereof include a large number of isomiR polynucleotides of SEQ ID NOs: 1 to 224 and 714 to 729 registered in miRBase. Examples of the polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 224 and 714 to 729 include a polynucleotide represented by any of SEQ ID NOs: 225 to 445 and 730 to 745, which are their respective precursors.

The names and miRBase Accession Nos. (registration numbers) of the genes represented by SEQ ID NOs: 1 to 765 are shown in Table 1.

As used herein, the term "capable of specifically binding" means that the nucleic acid probe or the primer used in the present invention binds to a particular target nucleic acid and cannot substantially bind to other nucleic acids.

TABLE 1

SEQ ID NO:	Gene name	miRBase registration No.
1	hsa-miR-1343-3p	MIMAT0019776
2	hsa-miR-6726-5p	MIMAT0027353
3	hsa-miR-6515-3p	MIMAT0025487
4	hsa-miR-4651	MIMAT0019715
5	hsa-miR-4257	MIMAT0016878
6	hsa-miR-3188	MIMAT0015070
7	hsa-miR-6131	MIMAT0024615
8	hsa-miR-6766-3p	MIMAT0027433
9	hsa-miR-7641	MIMAT0029782
10	hsa-miR-1249	MIMAT0005901
11	hsa-miR-3679-3p	MIMAT0018105
12	hsa-miR-6787-5p	MIMAT0027474
13	hsa-miR-4454	MIMAT0018976
14	hsa-miR-3135b	MIMAT0018985
15	hsa-miR-6765-3p	MIMAT0027431
16	hsa-miR-7975	MIMAT0031178
17	hsa-miR-204-3p	MIMAT0022693
18	hsa-miR-7977	MIMAT0031180
19	hsa-miR-7110-5p	MIMAT0028117
20	hsa-miR-6717-5p	MIMAT0025846
21	hsa-miR-6870-5p	MIMAT0027640
22	hsa-miR-663b	MIMAT0005867
23	hsa-miR-6875-5p	MIMAT0027650
24	hsa-miR-8072	MIMAT0030999
25	hsa-miR-6816-5p	MIMAT0027532
26	hsa-miR-4281	MIMAT0016907
27	hsa-miR-6729-5p	MIMAT0027359
28	hsa-miR-8069	MIMAT0030996
29	hsa-miR-4706	MIMAT0019806
30	hsa-miR-7108-5p	MIMAT0028113
31	hsa-miR-4433b-3p	MIMAT0030414
32	hsa-miR-6893-5p	MIMAT0027686
33	hsa-miR-6857-5p	MIMAT0027614
34	hsa-miR-1227-5p	MIMAT0022941
35	hsa-miR-6741-5p	MIMAT0027383
36	hsa-miR-451a	MIMAT0001631
37	hsa-miR-8063	MIMAT0030990
38	hsa-miR-3622a-5p	MIMAT0018003
39	hsa-miR-615-5p	MIMAT0004804
40	hsa-miR-128-1-5p	MIMAT0026477
41	hsa-miR-6825-5p	MIMAT0027550
42	hsa-miR-1260b	MIMAT0015041
43	hsa-miR-4433-3p	MIMAT0018949
44	hsa-miR-4665-5p	MIMAT0019739
45	hsa-miR-7845-5p	MIMAT0030420
46	hsa-miR-1908-5p	MIMAT0007881
47	hsa-miR-6840-3p	MIMAT0027583
48	hsa-miR-6765-5p	MIMAT0027430
49	hsa-miR-296-5p	MIMAT0000690
50	hsa-miR-3675-3p	MIMAT0018099
51	hsa-miR-6781-5p	MIMAT0027462
52	hsa-miR-423-5p	MIMAT0004748
53	hsa-miR-3663-3p	MIMAT0018085
54	hsa-miR-6784-5p	MIMAT0027468
55	hsa-miR-6749-5p	MIMAT0027398
56	hsa-miR-1231	MIMAT0005586
57	hsa-miR-4746-3p	MIMAT0019881
58	hsa-miR-6780b-5p	MIMAT0027572
59	hsa-miR-4758-5p	MIMAT0019903
60	hsa-miR-3679-5p	MIMAT0018104
61	hsa-miR-3184-5p	MIMAT0015064
62	hsa-miR-6125	MIMAT0024598
63	hsa-miR-6721-5p	MIMAT0025852
64	hsa-miR-6791-5p	MIMAT0027482
65	hsa-miR-3185	MIMAT0015065
66	hsa-miR-1260a	MIMAT0005911
67	hsa-miR-3197	MIMAT0015082
68	hsa-miR-6845-5p	MIMAT0027590
69	hsa-miR-6887-5p	MIMAT0027674
70	hsa-miR-6738-5p	MIMAT0027377
71	hsa-miR-6872-3p	MIMAT0027645
72	hsa-miR-4497	MIMAT0019032
73	hsa-miR-1229-5p	MIMAT0022942
74	hsa-miR-6820-5p	MIMAT0027540
75	hsa-miR-6777-5p	MIMAT0027454
76	hsa-miR-3917	MIMAT0018191
77	hsa-miR-5787	MIMAT0023252
78	hsa-miR-4286	MIMAT0016916
79	hsa-miR-6877-5p	MIMAT0027654
80	hsa-miR-1225-3p	MIMAT0005573

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
81	hsa-miR-6088	MIMAT0023713
82	hsa-miR-6800-5p	MIMAT0027500
83	hsa-miR-1246	MIMAT0005898
84	hsa-miR-4467	MIMAT0018994
85	hsa-miR-4419b	MIMAT0019034
86	hsa-miR-1914-3p	MIMAT0007890
87	hsa-miR-4632-5p	MIMAT0022977
88	hsa-miR-1915-5p	MIMAT0007891
89	hsa-miR-3940-5p	MIMAT0019229
90	hsa-miR-1185-2-3p	MIMAT0022713
91	hsa-miR-6746-5p	MIMAT0027392
92	hsa-miR-5001-5p	MIMAT0021021
93	hsa-miR-1228-5p	MIMAT0005582
94	hsa-miR-5572	MIMAT0022260
95	hsa-miR-4327	MIMAT0016889
96	hsa-miR-4638-5p	MIMAT0019695
97	hsa-miR-6799-5p	MIMAT0027498
98	hsa-miR-6861-5p	MIMAT0027623
99	hsa-miR-6727-5p	MIMAT0027355
100	hsa-miR-4513	MIMAT0019050
101	hsa-miR-6805-3p	MIMAT0027511
102	hsa-miR-6808-5p	MIMAT0027516
103	hsa-miR-4449	MIMAT0018968
104	hsa-miR-1199-5p	MIMAT0031119
105	hsa-miR-1275	MIMAT0005929
106	hsa-miR-4792	MIMAT0019964
107	hsa-miR-4443	MIMAT0018961
108	hsa-miR-6891-5p	MIMAT0027682
109	hsa-miR-6826-5p	MIMAT0027552
110	hsa-miR-6807-5p	MIMAT0027514
111	hsa-miR-7150	MIMAT0028211
112	hsa-miR-4534	MIMAT0019073
113	hsa-miR-4476	MIMAT0019003
114	hsa-miR-4649-5p	MIMAT0019711
115	hsa-miR-4525	MIMAT0019064
116	hsa-miR-1915-3p	MIMAT0007892
117	hsa-miR-4516	MIMAT0019053
118	hsa-miR-4417	MIMAT0018929
119	hsa-miR-642b-3p	MIMAT0018444
120	hsa-miR-3141	MIMAT0015010
121	hsa-miR-5100	MIMAT0022259
122	hsa-miR-6848-5p	MIMAT0027596
123	hsa-miR-4739	MIMAT0019868
124	hsa-miR-4459	MIMAT0018981
125	hsa-miR-1237-5p	MIMAT0022946
126	hsa-miR-296-3p	MIMAT0004679
127	hsa-miR-4665-3p	MIMAT0019740
128	hsa-miR-6786-5p	MIMAT0027472
129	hsa-miR-4258	MIMAT0016879
130	hsa-miR-6510-5p	MIMAT0025476
131	hsa-miR-1343-5p	MIMAT0027038
132	hsa-miR-1247-3p	MIMAT0022721
133	hsa-miR-6805-5p	MIMAT0027510
134	hsa-miR-4492	MIMAT0019027
135	hsa-miR-1469	MIMAT0007347
136	hsa-miR-1268b	MIMAT0018925
137	hsa-miR-6858-5p	MIMAT0027616
138	hsa-miR-3937	MIMAT0018352
139	hsa-miR-939-5p	MIMAT0004982
140	hsa-miR-3656	MIMAT0018076
141	hsa-miR-744-5p	MIMAT0004945
142	hsa-miR-4687-3p	MIMAT0019775
143	hsa-miR-4763-3p	MIMAT0019913
144	hsa-miR-3620-5p	MIMAT0022967
145	hsa-miR-3195	MIMAT0015079
146	hsa-miR-6842-5p	MIMAT0027586
147	hsa-miR-4707-5p	MIMAT0019807
148	hsa-miR-642a-3p	MIMAT0020924
149	hsa-miR-7113-3p	MIMAT0028124
150	hsa-miR-4728-5p	MIMAT0019849
151	hsa-miR-5195-3p	MIMAT0021127
152	hsa-miR-1185-1-3p	MIMAT0022838
153	hsa-miR-6774-5p	MIMAT0027448
154	hsa-miR-8059	MIMAT0030986
155	hsa-miR-3131	MIMAT0014996
156	hsa-miR-7847-3p	MIMAT0030422
157	hsa-miR-4463	MIMAT0018987

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
158	hsa-miR-128-2-5p	MIMAT0031095
159	hsa-miR-4508	MIMAT0019045
160	hsa-miR-6806-5p	MIMAT0027512
161	hsa-miR-7111-5p	MIMAT0028119
162	hsa-miR-6782-5p	MIMAT0027464
163	hsa-miR-4734	MIMAT0019859
164	hsa-miR-3162-5p	MIMAT0015036
165	hsa-miR-887-3p	MIMAT0004951
166	hsa-miR-6752-5p	MIMAT0027404
167	hsa-miR-6724-5p	MIMAT0025856
168	hsa-miR-23b-3p	MIMAT0000418
169	hsa-miR-23a-3p	MIMAT0000078
170	hsa-miR-625-3p	MIMAT0004808
171	hsa-miR-1228-3p	MIMAT0005583
172	hsa-miR-614	MIMAT0003282
173	hsa-miR-1913	MIMAT0007888
174	hsa-miR-92a-2-5p	MIMAT0004508
175	hsa-miR-187-5p	MIMAT0004561
176	hsa-miR-16-5p	MIMAT0000069
177	hsa-miR-92b-3p	MIMAT0003218
178	hsa-miR-150-3p	MIMAT0004610
179	hsa-miR-564	MIMAT0003228
180	hsa-miR-125a-3p	MIMAT0004602
181	hsa-miR-92b-5p	MIMAT0004792
182	hsa-miR-92a-3p	MIMAT0000092
183	hsa-miR-663a	MIMAT0003326
184	hsa-miR-4688	MIMAT0019777
185	hsa-miR-4648	MIMAT0019710
186	hsa-miR-6085	MIMAT0023710
187	hsa-miR-6126	MIMAT0024599
188	hsa-miR-6880-5p	MIMAT0027660
189	hsa-miR-328-5p	MIMAT0026486
190	hsa-miR-6768-5p	MIMAT0027436
191	hsa-miR-3180	MIMAT0018178
192	hsa-miR-6087	MIMAT0023712
193	hsa-miR-1273g-3p	MIMAT0022742
194	hsa-miR-1225-5p	MIMAT0005572
195	hsa-miR-3196	MIMAT0015080
196	hsa-miR-4695-5p	MIMAT0019788
197	hsa-miR-6732-5p	MIMAT0027365
198	hsa-miR-638	MIMAT0003308
199	hsa-miR-6813-5p	MIMAT0027526
200	hsa-miR-665	MIMAT0004952
201	hsa-miR-486-3p	MIMAT0004762
202	hsa-miR-4466	MIMAT0018993
203	hsa-miR-30c-1-3p	MIMAT0004674
204	hsa-miR-3621	MIMAT0018002
205	hsa-miR-6743-5p	MIMAT0027387
206	hsa-miR-4298	MIMAT0016852
207	hsa-miR-4741	MIMAT0019871
208	hsa-miR-3619-3p	MIMAT0019219
209	hsa-miR-6824-5p	MIMAT0027548
210	hsa-miR-5698	MIMAT0022491
211	hsa-miR-371a-5p	MIMAT0004687
212	hsa-miR-4488	MIMAT0019022
213	hsa-miR-1233-5p	MIMAT0022943
214	hsa-miR-4723-5p	MIMAT0019838
215	hsa-miR-24-3p	MIMAT0000080
216	hsa-miR-1238-5p	MIMAT0022947
217	hsa-miR-4442	MIMAT0018960
218	hsa-miR-3928-3p	MIMAT0018205
219	hsa-miR-6716-5p	MIMAT0025844
220	hsa-miR-6089	MIMAT0023714
221	hsa-miR-6124	MIMAT0024597
222	hsa-miR-6778-5p	MIMAT0027456
223	hsa-miR-557	MIMAT0003221
224	hsa-miR-6090	MIMAT0023715
225	hsa-mir-1343	MI0017320
226	hsa-mir-6726	MI0022571
227	hsa-mir-6515	MI0022227
228	hsa-mir-4651	MI0017279
229	hsa-mir-4257	MI0015856
230	hsa-mir-3188	MI0014232
231	hsa-mir-6131	MI0021276
232	hsa-mir-6766	MI0022611
233	hsa-mir-7641-1	MI0024975
234	hsa-mir-7641-2	MI0024976

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
235	hsa-mir-1249	MI0006384
236	hsa-mir-3679	MI0016080
237	hsa-mir-6787	MI0022632
238	hsa-mir-4454	MI0016800
239	hsa-mir-3135b	MI0016809
240	hsa-mir-6765	MI0022610
241	hsa-mir-7975	MI0025751
242	hsa-mir-204	MI0000284
243	hsa-mir-7977	MI0025753
244	hsa-mir-7110	MI0022961
245	hsa-mir-6717	MI0022551
246	hsa-mir-6870	MI0022717
247	hsa-mir-663b	MI0006336
248	hsa-mir-6875	MI0022722
249	hsa-mir-8072	MI0025908
250	hsa-mir-6816	MI0022661
251	hsa-mir-4281	MI0015885
252	hsa-mir-6729	MI0022574
253	hsa-mir-8069	MI0025905
254	hsa-mir-4706	MI0017339
255	hsa-mir-7108	MI0022959
256	hsa-mir-4433b	MI0025511
257	hsa-mir-6893	MI0022740
258	hsa-mir-6857	MI0022703
259	hsa-mir-1227	MI0006316
260	hsa-mir-6741	MI0022586
261	hsa-mir-451a	MI0001729
262	hsa-mir-8063	MI0025899
263	hsa-mir-3622a	MI0016013
264	hsa-mir-615	MI0003628
265	hsa-mir-128-1	MI0000447
266	hsa-mir-6825	MI0022670
267	hsa-mir-1260b	MI0014197
268	hsa-mir-4433	MI0016773
269	hsa-mir-4665	MI0017295
270	hsa-mir-7845	MI0025515
271	hsa-mir-1908	MI0008329
272	hsa-mir-6840	MI0022686
240	hsa-mir-6765	MI0022610
273	hsa-mir-296	MI0000747
274	hsa-mir-3675	MI0016076
275	hsa-mir-6781	MI0022626
276	hsa-mir-423	MI0001445
277	hsa-mir-3663	MI0016064
278	hsa-mir-6784	MI0022629
279	hsa-mir-6749	MI0022594
280	hsa-mir-1231	MI0006321
281	hsa-mir-4746	MI0017385
282	hsa-mir-6780b	MI0022681
283	hsa-mir-4758	MI0017399
236	hsa-mir-3679	MI0016080
284	hsa-mir-3184	MI0014226
285	hsa-mir-6125	MI0021259
286	hsa-mir-6721	MI0022556
287	hsa-mir-6791	MI0022636
288	hsa-mir-3185	MI0014227
289	hsa-mir-1260a	MI0006394
290	hsa-mir-3197	MI0014245
291	hsa-mir-6845	MI0022691
292	hsa-mir-6887	MI0022734
293	hsa-mir-6738	MI0022583
294	hsa-mir-6872	MI0022719
295	hsa-mir-4497	MI0016859
296	hsa-mir-1229	MI0006319
297	hsa-mir-6820	MI0022665
298	hsa-mir-6777	MI0022622
299	hsa-mir-3917	MI0016423
300	hsa-mir-5787	MI0019797
301	hsa-mir-4286	MI0015894
302	hsa-mir-6877	MI0022724
303	hsa-mir-1225	MI0006311
304	hsa-mir-6088	MI0020365
305	hsa-mir-6800	MI0022645
306	hsa-mir-1246	MI0006381
307	hsa-mir-4467	MI0016818
308	hsa-mir-4419b	MI0016861
309	hsa-mir-1914	MI0008335

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
310	hsa-mir-4632	MI0017259
311	hsa-mir-1915	MI0008336
312	hsa-mir-3940	MI0016597
313	hsa-mir-1185-2	MI0003821
314	hsa-mir-6746	MI0022591
315	hsa-mir-5001	MI0017867
316	hsa-mir-1228	MI0006318
317	hsa-mir-5572	MI0019117
318	hsa-mir-4327	MI0015867
319	hsa-mir-4638	MI0017265
320	hsa-mir-6799	MI0022644
321	hsa-mir-6861	MI0022708
322	hsa-mir-6727	MI0022572
323	hsa-mir-4513	MI0016879
324	hsa-mir-6805	MI0022650
325	hsa-mir-6808	MI0022653
326	hsa-mir-4449	MI0016792
327	hsa-mir-1199	MI0020340
328	hsa-mir-1275	MI0006415
329	hsa-mir-4792	MI0017439
330	hsa-mir-4443	MI0016786
331	hsa-mir-6891	MI0022738
332	hsa-mir-6826	MI0022671
333	hsa-mir-6807	MI0022652
334	hsa-mir-7150	MI0023610
335	hsa-mir-4534	MI0016901
336	hsa-mir-4476	MI0016828
337	hsa-mir-4649	MI0017276
338	hsa-mir-4525	MI0016892
311	hsa-mir-1915	MI0008336
339	hsa-mir-4516	MI0016882
340	hsa-mir-4417	MI0016753
341	hsa-mir-642b	MI0016685
342	hsa-mir-3141	MI0014165
343	hsa-mir-5100	MI0019116
344	hsa-mir-6848	MI0022694
345	hsa-mir-4739	MI0017377
346	hsa-mir-4459	MI0016805
347	hsa-mir-1237	MI0006327
273	hsa-mir-296	MI0000747
269	hsa-mir-4665	MI0017295
348	hsa-mir-6786	MI0022631
349	hsa-mir-4258	MI0015857
350	hsa-mir-6510	MI0022222
225	hsa-mir-1343	MI0017320
351	hsa-mir-1247	MI0006382
324	hsa-mir-6805	MI0022650
352	hsa-mir-4492	MI0016854
353	hsa-mir-1469	MI0007074
354	hsa-mir-1268b	MI0016748
355	hsa-mir-6858	MI0022704
356	hsa-mir-3937	MI0016593
357	hsa-mir-939	MI0005761
358	hsa-mir-3656	MI0016056
359	hsa-mir-744	MI0005559
360	hsa-mir-4687	MI0017319
361	hsa-mir-4763	MI0017404
362	hsa-mir-3620	MI0016011
363	hsa-mir-3195	MI0014240
364	hsa-mir-6842	MI0022688
365	hsa-mir-4707	MI0017340
366	hsa-mir-642a	MI0003657
367	hsa-mir-7113	MI0022964
368	hsa-mir-4728	MI0017365
369	hsa-mir-5195	MI0018174
370	hsa-mir-1185-1	MI0003844
371	hsa-mir-6774	MI0022619
372	hsa-mir-8059	MI0025895
373	hsa-mir-3131	MI0014151
374	hsa-mir-7847	MI0025517
375	hsa-mir-4463	MI0016811
376	hsa-mir-128-2	MI0000727
377	hsa-mir-4508	MI0016872
378	hsa-mir-6806	MI0022651
379	hsa-mir-7111	MI0022962
380	hsa-mir-6782	MI0022627
381	hsa-mir-4734	MI0017371

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
382	hsa-mir-3162	MI0014192
383	hsa-mir-887	MI0005562
384	hsa-mir-6752	MI0022597
385	hsa-mir-6724	MI0022559
386	hsa-mir-23b	MI0000439
387	hsa-mir-23a	MI0000079
388	hsa-mir-625	MI0003639
316	hsa-mir-1228	MI0006318
389	hsa-mir-614	MI0003627
390	hsa-mir-1913	MI0008334
391	hsa-mir-92a-2	MI0000094
392	hsa-mir-187	MI0000274
393	hsa-mir-16-1	MI0000070
394	hsa-mir-16-2	MI0000115
395	hsa-mir-92b	MI0003560
396	hsa-mir-150	MI0000479
397	hsa-mir-564	MI0003570
398	hsa-mir-125a	MI0000469
395	hsa-mir-92b	MI0003560
399	hsa-mir-92a-1	MI0000093
391	hsa-mir-92a-2	MI0000094
400	hsa-mir-663a	MI0003672
401	hsa-mir-4688	MI0017321
402	hsa-mir-4648	MI0017275
403	hsa-mir-6085	MI0020362
404	hsa-mir-6126	MI0021260
405	hsa-mir-6880	MI0022727
406	hsa-mir-328	MI0000804
407	hsa-mir-6768	MI0022613
408	hsa-mir-3180-4	MI0016408
409	hsa-mir-3180-5	MI0016409
410	hsa-mir-6087	MI0020364
411	hsa-mir-1273g	MI0018003
303	hsa-mir-1225	MI0006311
412	hsa-mir-3196	MI0014241
413	hsa-mir-4695	MI0017328
414	hsa-mir-6732	MI0022577
415	hsa-mir-638	MI0003653
416	hsa-mir-6813	MI0022658
417	hsa-mir-665	MI0005563
418	hsa-mir-486	MI0002470
419	hsa-mir-486-2	MI0023622
420	hsa-mir-4466	MI0016817
421	hsa-mir-30c-1	MI0000736
422	hsa-mir-3621	MI0016012
423	hsa-mir-6743	MI0022588
424	hsa-mir-4298	MI0015830
425	hsa-mir-4741	MI0017379
426	hsa-mir-3619	MI0016009
427	hsa-mir-6824	MI0022669
428	hsa-mir-5698	MI0019305
429	hsa-mir-371a	MI0000779
430	hsa-mir-4488	MI0016849
431	hsa-mir-1233-1	MI0006323
432	hsa-mir-1233-2	MI0015973
433	hsa-mir-4723	MI0017359
434	hsa-mir-24-1	MI0000080
435	hsa-mir-24-2	MI0000081
436	hsa-mir-1238	MI0006328
437	hsa-mir-4442	MI0016785
438	hsa-mir-3928	MI0016438
439	hsa-mir-6716	MI0022550
440	hsa-mir-6089-1	MI0020366
441	hsa-mir-6089-2	MI0023563
442	hsa-mir-6124	MI0021258
443	hsa-mir-6778	MI0022623
444	hsa-mir-557	MI0003563
445	hsa-mir-6090	MI0020367
446	isomiR example 1 of SEQ ID NO: 1	—
447	isomiR example 2 of SEQ ID NO: 1	—
448	isomiR example 1 of SEQ ID NO: 3	—
449	isomiR example 2 of SEQ ID NO: 3	—
450	isomiR example 1 of SEQ ID NO: 4	—
451	isomiR example 2 of SEQ ID NO: 4	—
452	isomiR example 1 of SEQ ID NO: 6	—
453	isomiR example 2 of SEQ ID NO: 6	—
454	isomiR example 1 of SEQ ID NO: 7	—

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
455	isomiR example 2 of SEQ ID NO: 7	—
456	isomiR example 1 of SEQ ID NO: 10	—
457	isomiR example 2 of SEQ ID NO: 10	—
458	isomiR example 1 of SEQ ID NO: 11	—
459	isomiR example 2 of SEQ ID NO: 11	—
460	isomiR example 1 of SEQ ID NO: 13	—
461	isomiR example 2 of SEQ ID NO: 13	—
462	isomiR example 1 of SEQ ID NO: 14	—
463	isomiR example 2 of SEQ ID NO: 14	—
464	isomiR example 1 of SEQ ID NO: 16	—
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466	isomiR example 1 of SEQ ID NO: 17	—
467	isomiR example 2 of SEQ ID NO: 17	—
468	isomiR example 1 of SEQ ID NO: 20	—
469	isomiR example 2 of SEQ ID NO: 20	—
470	isomiR example 1 of SEQ ID NO: 22	—
471	isomiR example 2 of SEQ ID NO: 22	—
472	isomiR example 1 of SEQ ID NO: 26	—
473	isomiR example 2 of SEQ ID NO: 26	—
474	isomiR example 1 of SEQ ID NO: 29	—
475	isomiR example 2 of SEQ ID NO: 29	—
476	isomiR example 1 of SEQ ID NO: 36	—
477	isomiR example 2 of SEQ ID NO: 36	—
478	isomiR example 1 of SEQ ID NO: 38	—
479	isomiR example 2 of SEQ ID NO: 38	—
480	isomiR example 1 of SEQ ID NO: 39	—
481	isomiR example 2 of SEQ ID NO: 39	—
482	isomiR example 1 of SEQ ID NO: 40	—
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527	isomiR example 2 of SEQ ID NO: 86	—
528	isomiR example 1 of SEQ ID NO: 87	—
529	isomiR example 2 of SEQ ID NO: 87	—
530	isomiR example 1 of SEQ ID NO: 88	—
531	isomiR example 2 of SEQ ID NO: 88	—

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
532	isomiR example 1 of SEQ ID NO: 89	—
533	isomiR example 2 of SEQ ID NO: 89	—
534	isomiR example 1 of SEQ ID NO: 90	—
535	isomiR example 2 of SEQ ID NO: 90	—
536	isomiR example 1 of SEQ ID NO: 92	—
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538	isomiR example 1 of SEQ ID NO: 93	—
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540	isomiR example 1 of SEQ ID NO: 94	—
541	isomiR example 2 of SEQ ID NO: 94	—
542	isomiR example 1 of SEQ ID NO: 96	—
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546	isomiR example 1 of SEQ ID NO: 103	—
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556	isomiR example 1 of SEQ ID NO: 114	—
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560	isomiR example 1 of SEQ ID NO: 116	—
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562	isomiR example 1 of SEQ ID NO: 117	—
563	isomiR example 2 of SEQ ID NO: 117	—
564	isomiR example 1 of SEQ ID NO: 118	—
565	isomiR example 2 of SEQ ID NO: 118	—
566	isomiR example 1 of SEQ ID NO: 119	—
567	isomiR example 2 of SEQ ID NO: 119	—
568	isomiR example 1 of SEQ ID NO: 120	—
569	isomiR example 2 of SEQ ID NO: 120	—
570	isomiR example 1 of SEQ ID NO: 121	—
571	isomiR example 2 of SEQ ID NO: 121	—
572	isomiR example 1 of SEQ ID NO: 123	—
573	isomiR example 2 of SEQ ID NO: 123	—
574	isomiR example 1 of SEQ ID NO: 124	—
575	isomiR example 2 of SEQ ID NO: 124	—
576	isomiR example 1 of SEQ ID NO: 125	—
577	isomiR example 2 of SEQ ID NO: 125	—
578	isomiR example 1 of SEQ ID NO: 126	—
579	isomiR example 2 of SEQ ID NO: 126	—
580	isomiR example 1 of SEQ ID NO: 130	—
581	isomiR example 2 of SEQ ID NO: 130	—
582	isomiR example 1 of SEQ ID NO: 132	—
583	isomiR example 2 of SEQ ID NO: 132	—
584	isomiR example 1 of SEQ ID NO: 134	—
585	isomiR example 2 of SEQ ID NO: 134	—
586	isomiR example 1 of SEQ ID NO: 136	—
587	isomiR example 2 of SEQ ID NO: 136	—
588	isomiR example 1 of SEQ ID NO: 139	—
589	isomiR example 2 of SEQ ID NO: 139	—
590	isomiR example 1 of SEQ ID NO: 140	—
591	isomiR example 2 of SEQ ID NO: 140	—
592	isomiR example 1 of SEQ ID NO: 141	—
593	isomiR example 2 of SEQ ID NO: 141	—
594	isomiR example 1 of SEQ ID NO: 142	—
595	isomiR example 2 of SEQ ID NO: 142	—
596	isomiR example 1 of SEQ ID NO: 143	—
597	isomiR example 2 of SEQ ID NO: 143	—
598	isomiR example 1 of SEQ ID NO: 144	—
599	isomiR example 2 of SEQ ID NO: 144	—
600	isomiR example 1 of SEQ ID NO: 145	—
601	isomiR example 2 of SEQ ID NO: 145	—
602	isomiR example 1 of SEQ ID NO: 147	—
603	isomiR example 2 of SEQ ID NO: 147	—
604	isomiR example 1 of SEQ ID NO: 148	—
605	isomiR example 2 of SEQ ID NO: 148	—
606	isomiR example 1 of SEQ ID NO: 150	—
607	isomiR example 2 of SEQ ID NO: 150	—
608	isomiR example 1 of SEQ ID NO: 151	—

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
609	isomiR example 2 of SEQ ID NO: 151	—
610	isomiR example 1 of SEQ ID NO: 152	—
611	isomiR example 2 of SEQ ID NO: 152	—
612	isomiR example 1 of SEQ ID NO: 155	—
613	isomiR example 2 of SEQ ID NO: 155	—
614	isomiR example 1 of SEQ ID NO: 157	—
615	isomiR example 2 of SEQ ID NO: 157	—
616	isomiR example 1 of SEQ ID NO: 158	—
617	isomiR example 2 of SEQ ID NO: 158	—
618	isomiR example 1 of SEQ ID NO: 159	—
619	isomiR example 2 of SEQ ID NO: 159	—
620	isomiR example 1 of SEQ ID NO: 163	—
621	isomiR example 2 of SEQ ID NO: 163	—
622	isomiR example 1 of SEQ ID NO: 164	—
623	isomiR example 2 of SEQ ID NO: 164	—
624	isomiR example 1 of SEQ ID NO: 165	—
625	isomiR example 2 of SEQ ID NO: 165	—
626	isomiR example 1 of SEQ ID NO: 167	—
627	isomiR example 2 of SEQ ID NO: 167	—
628	isomiR example 1 of SEQ ID NO: 168	—
629	isomiR example 2 of SEQ ID NO: 168	—
630	isomiR example 1 of SEQ ID NO: 169	—
631	isomiR example 2 of SEQ ID NO: 169	—
632	isomiR example 1 of SEQ ID NO: 170	—
633	isomiR example 2 of SEQ ID NO: 170	—
634	isomiR example 1 of SEQ ID NO: 171	—
635	isomiR example 2 of SEQ ID NO: 171	—
636	isomiR example 1 of SEQ ID NO: 172	—
637	isomiR example 2 of SEQ ID NO: 172	—
638	isomiR example 1 of SEQ ID NO: 173	—
639	isomiR example 2 of SEQ ID NO: 173	—
640	isomiR example 1 of SEQ ID NO: 174	—
641	isomiR example 2 of SEQ ID NO: 174	—
642	isomiR example 1 of SEQ ID NO: 175	—
643	isomiR example 2 of SEQ ID NO: 175	—
644	isomiR example 1 of SEQ ID NO: 176	—
645	isomiR example 2 of SEQ ID NO: 176	—
646	isomiR example 1 of SEQ ID NO: 177	—
647	isomiR example 2 of SEQ ID NO: 177	—
648	isomiR example 1 of SEQ ID NO: 178	—
649	isomiR example 2 of SEQ ID NO: 178	—
650	isomiR example 1 of SEQ ID NO: 179	—
651	isomiR example 2 of SEQ ID NO: 179	—
652	isomiR example 1 of SEQ ID NO: 180	—
653	isomiR example 2 of SEQ ID NO: 180	—
654	isomiR example 1 of SEQ ID NO: 181	—
655	isomiR example 2 of SEQ ID NO: 181	—
656	isomiR example 1 of SEQ ID NO: 182	—
657	isomiR example 2 of SEQ ID NO: 182	—
658	isomiR example 1 of SEQ ID NO: 183	—
659	isomiR example 2 of SEQ ID NO: 183	—
660	isomiR example 1 of SEQ ID NO: 184	—
661	isomiR example 2 of SEQ ID NO: 184	—
662	isomiR example 1 of SEQ ID NO: 185	—
663	isomiR example 2 of SEQ ID NO: 185	—
664	isomiR example 1 of SEQ ID NO: 187	—
665	isomiR example 2 of SEQ ID NO: 187	—
666	isomiR example 1 of SEQ ID NO: 189	—
667	isomiR example 2 of SEQ ID NO: 189	—
668	isomiR example 1 of SEQ ID NO: 191	—
669	isomiR example 2 of SEQ ID NO: 191	—
670	isomiR example 1 of SEQ ID NO: 192	—
671	isomiR example 2 of SEQ ID NO: 192	—
672	isomiR example 1 of SEQ ID NO: 193	—
673	isomiR example 2 of SEQ ID NO: 193	—
674	isomiR example 1 of SEQ ID NO: 195	—
675	isomiR example 2 of SEQ ID NO: 195	—
676	isomiR example 1 of SEQ ID NO: 196	—
677	isomiR example 2 of SEQ ID NO: 196	—
678	isomiR example 1 of SEQ ID NO: 198	—
679	isomiR example 2 of SEQ ID NO: 198	—
680	isomiR example 1 of SEQ ID NO: 200	—
681	isomiR example 2 of SEQ ID NO: 200	—
682	isomiR example 1 of SEQ ID NO: 201	—
683	isomiR example 2 of SEQ ID NO: 201	—
684	isomiR example 1 of SEQ ID NO: 202	—
685	isomiR example 2 of SEQ ID NO: 202	—

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
686	isomiR example 1 of SEQ ID NO: 203	—
687	isomiR example 2 of SEQ ID NO: 203	—
688	isomiR example 1 of SEQ ID NO: 206	—
689	isomiR example 2 of SEQ ID NO: 206	—
690	isomiR example 1 of SEQ ID NO: 207	—
691	isomiR example 2 of SEQ ID NO: 207	—
692	isomiR example 1 of SEQ ID NO: 210	—
693	isomiR example 2 of SEQ ID NO: 210	—
694	isomiR example 1 of SEQ ID NO: 211	—
695	isomiR example 2 of SEQ ID NO: 211	—
696	isomiR example 1 of SEQ ID NO: 212	—
697	isomiR example 2 of SEQ ID NO: 212	—
698	isomiR example 1 of SEQ ID NO: 213	—
699	isomiR example 2 of SEQ ID NO: 213	—
700	isomiR example 1 of SEQ ID NO: 214	—
701	isomiR example 2 of SEQ ID NO: 214	—
702	isomiR example 1 of SEQ ID NO: 215	—
703	isomiR example 2 of SEQ ID NO: 215	—
704	isomiR example 1 of SEQ ID NO: 217	—
705	isomiR example 2 of SEQ ID NO: 217	—
706	isomiR example 1 of SEQ ID NO: 218	—
707	isomiR example 2 of SEQ ID NO: 218	—
708	isomiR example 1 of SEQ ID NO: 219	—
709	isomiR example 2 of SEQ ID NO: 219	—
710	isomiR example 1 of SEQ ID NO: 220	—
711	isomiR example 2 of SEQ ID NO: 220	—
712	isomiR example 1 of SEQ ID NO: 221	—
713	isomiR example 2 of SEQ ID NO: 221	—
714	hsa-miR-6757-5p	MIMAT0027414
715	hsa-miR-4448	MIMAT0018967
716	hsa-miR-671-5p	MIMAT0003880
717	hsa-miR-3178	MIMAT0015055
718	hsa-miR-4725-3p	MIMAT0019844
719	hsa-miR-940	MIMAT0004983
720	hsa-miR-6789-5p	MIMAT0027478
721	hsa-miR-4484	MIMAT0019018
722	hsa-miR-4634	MIMAT0019691
723	hsa-miR-4745-5p	MIMAT0019878
724	hsa-miR-4730	MIMAT0019852
725	hsa-miR-6803-5p	MIMAT0027506
726	hsa-miR-6798-5p	MIMAT0027496
727	hsa-miR-3648	MIMAT0018068
728	hsa-miR-4783-3p	MIMAT0019947
729	hsa-miR-6836-3p	MIMAT0027575
730	hsa-mir-6757	MI0022602
731	hsa-mir-4448	MI0016791
732	hsa-mir-671	MI0003760
733	hsa-mir-3178	MI0014212
734	hsa-mir-4725	MI0017362
735	hsa-mir-940	MI0005762
736	hsa-mir-6789	MI0022634
737	hsa-mir-4484	MI0016845
738	hsa-mir-4634	MI0017261
739	hsa-mir-4745	MI0017384
740	hsa-mir-4730	MI0017367
741	hsa-mir-6803	MI0022648
742	hsa-mir-6798	MI0022643
743	hsa-mir-3648	MI0016048
744	hsa-mir-4783	MI0017428
745	hsa-mir-6836	MI0022682
746	isomiR example 1 of SEQ ID NO: 715	—
747	isomiR example 2 of SEQ ID NO: 715	—
748	isomiR example 1 of SEQ ID NO: 716	—
749	isomiR example 2 of SEQ ID NO: 716	—
750	isomiR example 1 of SEQ ID NO: 717	—
751	isomiR example 2 of SEQ ID NO: 717	—
752	isomiR example 1 of SEQ ID NO: 718	—
753	isomiR example 2 of SEQ ID NO: 718	—
754	isomiR example 1 of SEQ ID NO: 719	—
755	isomiR example 2 of SEQ ID NO: 719	—
756	isomiR example 1 of SEQ ID NO: 721	—
757	isomiR example 2 of SEQ ID NO: 721	—
758	isomiR example 1 of SEQ ID NO: 723	—
759	isomiR example 2 of SEQ ID NO: 723	—
760	isomiR example 1 of SEQ ID NO: 724	—
761	isomiR example 2 of SEQ ID NO: 724	—
762	isomiR example 1 of SEQ ID NO: 727	—

TABLE 1-continued

SEQ ID NO:	Gene name	miRBase registration No.
763	isomiR example 2 of SEQ ID NO: 727	—
764	isomiR example 1 of SEQ ID NO: 728	—
765	isomiR example 2 of SEQ ID NO: 728	—

The present specification encompasses the contents described in the specifications and drawings of Japanese Patent Application Nos. 2014-124880 on which the priority of the present application is based.

Advantageous Effects of Invention

According to the present invention, liver cancer can be detected easily and highly accurately. For example, the presence or absence of liver cancer in a patient can be easily detected by using, as an indicator, the measurement values of several miRNAs in blood, serum, and/or plasma of the patient, which can be collected with limited invasiveness.

BRIEF DESCRIPTION OF DRAWINGS

FIG. **1** This figure shows the relationship between the nucleotide sequences of hsa-miR-1343-5p represented by SEQ ID NO: 131 and hsa-miR-1343-3p represented by SEQ ID NO: 1, which are produced from a precursor hsa-mir-1343 represented by SEQ ID NO: 225.

FIG. **2** Left diagram: the measurement values of hsa-miR-1343-3p (SEQ ID NO: 1) in healthy subjects (100 persons) and liver cancer patients (34 persons) selected as a training cohort were each plotted on the ordinate. The horizontal line in the diagram depicts a threshold (7.09) that was optimized by Fisher's linear discriminant analysis and discriminated between the two groups. Right diagram: the measurement values of hsa-miR-1343-3p (SEQ ID NO: 1) in healthy subjects (50 persons) and liver cancer patients (16 persons) selected as a validation cohort were each plotted on the ordinate. The horizontal line in the diagram depicts the threshold (7.09) that was set in the training cohort and discriminated between the two groups.

FIG. **3** Left diagram: the measurement values of hsa-miR-1343-3p (SEQ ID NO: 1) in healthy subjects (100 persons, circles) and liver cancer patients (34 persons, triangles) selected as a training cohort were each plotted on the abscissa against their measurement values of hsa-miR-6'726-5p (SEQ ID NO: 2) on the ordinate. The line in the diagram depicts a discriminant function (0=0.77x+y−15.07) that was optimized by Fisher's linear discriminant analysis and discriminated between the two groups. Right diagram: the measurement values of hsa-miR-1343-3p (SEQ ID NO: 1) in healthy subjects (50 persons, circles) and liver cancer patients (16 persons, triangles) selected as a validation cohort were each plotted on the abscissa against their measurement values of hsa-miR-6726-5p (SEQ ID NO: 2) on the ordinate. The line in the diagram depicts the threshold (0=0.77x+y−15.07) that was set in the training cohorts and discriminated between the two groups.

FIG. **4** Upper diagram: a discriminant (0.88×hsa-miR-6131-1.58×hsa-miR-642a-3p+0.39×hsa-miR-7641-0.33×hsa-miR-6729-5p+5.19) was prepared by use of Fisher's linear discriminant analysis from the measurement values of hsa-miR-6131 (SEQ ID NO: 7), hsa-miR-642a-3p (SEQ ID NO: 148), hsa-miR-7641 (SEQ ID NO: 9), and hsa-miR-6'729-5p (SEQ ID NO: 27) in 35 liver cancer patients, 99 healthy subjects, 72 pancreatic cancer patients, 61 bile duct

cancer patients, 35 colorectal cancer patients, 38 stomach cancer patients, 25 esophageal cancer patients, and 16 benign pancreaticobiliary disease patients selected as a training cohort, and discriminant scores obtained from the discriminant were plotted on the ordinate against the sample groups on the abscissa. The dotted line in the diagram depicts a discriminant boundary that offered a discriminant score of 0 and discriminated between the groups. Lower diagram: discriminant scores obtained from the discriminant prepared from the training cohorts as to the measurement values of hsa-miR-6131 (SEQ ID NO: 7), hsa-miR-642a-3p (SEQ ID NO: 148), hsa-miR-7641 (SEQ ID NO: 9), and hsa-miR-6729-5p (SEQ ID NO: 27) in 17 liver cancer patients, 51 healthy subjects, 28 pancreatic cancer patients, 37 bile duct cancer patients, 15 colorectal cancer patients, 12 stomach cancer patients, 25 esophageal cancer patients, and 5 benign pancreaticobiliary disease patients selected as a validation cohort were plotted on the ordinate against the sample groups on the abscissa. The dotted line in the diagram depicts the discriminant boundary that offered a discriminant score of 0 and discriminated between the two groups.

DESCRIPTION OF EMBODIMENTS

Hereinafter, the present invention will be further described specifically.

1. Target Nucleic Acid for Liver Cancer

As a primary target nucleic acid as a liver cancer marker for detecting the presence and/or absence of liver cancer or liver cancer cells using the nucleic acid probe or the primer for the detection of liver cancer defined above according to the present invention, at least one or more miRNA(s) selected from the group consisting of hsa-miR-1343-3p, hsa-miR-6726-5p, hsa-miR-6515-3p, hsa-miR-4651, hsa-miR-4257, hsa-miR-3188, hsa-miR-6131, hsa-miR-6766-3p, hsa-miR-7641, hsa-miR-1249, hsa-miR-3679-3p, hsa-miR-6787-5p, hsa-miR-4454, hsa-miR-3135b, hsa-miR-6765-3p, hsa-miR-7975, hsa-miR-204-3p, hsa-miR-7977, hsa-miR-7110-5p, hsa-miR-6717-5p, hsa-miR-6870-5p, hsa-miR-663b, hsa-miR-6875-5p, hsa-miR-8072, hsa-miR-6816-5p, hsa-miR-4281, hsa-miR-6729-5p, hsa-miR-8069, hsa-miR-4706, hsa-miR-7108-5p, hsa-miR-4433b-3p, hsa-miR-6893-5p, hsa-miR-6857-5p, hsa-miR-1227-5p, hsa-miR-6741-5p, hsa-miR-451a, hsa-miR-8063, hsa-miR-3622a-5p, hsa-miR-615-5p, hsa-miR-128-1-5p, hsa-miR-6825-5p, hsa-miR-1260b, hsa-miR-4433-3p, hsa-miR-4665-5p, hsa-miR-7845-5p, hsa-miR-1908-5p, hsa-miR-6840-3p, hsa-miR-6765-5p, hsa-miR-296-5p, hsa-miR-3675-3p, hsa-miR-6781-5p, hsa-miR-423-5p, hsa-miR-3663-3p, hsa-miR-6784-5p, hsa-miR-6749-5p, hsa-miR-1231, hsa-miR-4746-3p, hsa-miR-6780b-5p, hsa-miR-4758-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-6125, hsa-miR-6721-5p, hsa-miR-6791-5p, hsa-miR-3185, hsa-miR-1260a, hsa-miR-3197, hsa-miR-6845-5p, hsa-miR-6887-5p, hsa-miR-6738-5p, hsa-miR-6872-3p, hsa-miR-4497, hsa-miR-1229-5p, hsa-miR-6820-5p, hsa-miR-6777-5p, hsa-miR-3917, hsa-miR-5787, hsa-miR-4286, hsa-miR-6877-5p, hsa-miR-1225-3p, hsa-miR-6088, hsa-miR-6800-5p, hsa-miR-1246, hsa-miR-4467, hsa-miR-4419b, hsa-miR-1914-3p, hsa-miR-4632-5p, hsa-miR-1915-5p, hsa-miR-3940-5p, hsa-miR-1185-2-3p, hsa-miR-6746-5p, hsa-miR-5001-5p, hsa-miR-1228-5p, hsa-miR-5572, hsa-miR-4327, hsa-miR-4638-5p, hsa-miR-6799-5p, hsa-miR-6861-5p, hsa-miR-6727-5p, hsa-miR-4513, hsa-miR-6805-3p, hsa-miR-6808-5p, hsa-miR-4449, hsa-miR-1199-5p, hsa-miR-1275, hsa-miR-4792, hsa-miR-4443, hsa-miR-6891-5p, hsa-miR-6826-5p, hsa-miR-6807-5p, hsa-miR-7150, hsa-miR-4534, hsa-miR-4476, hsa-miR-4649-5p, hsa-miR-4525, hsa-miR-1915-3p, hsa-miR-4516, hsa-miR-4417, hsa-miR-642b-3p, hsa-miR-3141, hsa-miR-5100, hsa-miR-6848-5p, hsa-miR-4739, hsa-miR-4459, hsa-miR-1237-5p, hsa-miR-296-3p, hsa-miR-4665-3p, hsa-miR-6786-5p, hsa-miR-4258, hsa-miR-6510-5p, hsa-miR-1343-5p, hsa-miR-1247-3p, hsa-miR-6805-5p, hsa-miR-4492, hsa-miR-1469, hsa-miR-1268b, hsa-miR-6858-5p, hsa-miR-3937, hsa-miR-939-5p, hsa-miR-3656, hsa-miR-744-5p, hsa-miR-4687-3p, hsa-miR-4763-3p, hsa-miR-3620-5p, hsa-miR-3195, hsa-miR-6842-5p, hsa-miR-4707-5p, hsa-miR-642a-3p, hsa-miR-7113-3p, hsa-miR-4728-5p, hsa-miR-5195-3p, hsa-miR-1185-1-3p, hsa-miR-6774-5p, hsa-miR-8059, hsa-miR-3131, hsa-miR-7847-3p, hsa-miR-4463, hsa-miR-128-2-5p, hsa-miR-4508, hsa-miR-6806-5p, hsa-miR-7111-5p, hsa-miR-6782-5p, hsa-miR-4734, hsa-miR-3162-5p, hsa-miR-887-3p, hsa-miR-6752-5p, hsa-miR-6724-5p, hsa-miR-6757-5p, hsa-miR-4448, hsa-miR-671-5p, hsa-miR-3178, hsa-miR-4725-3p, hsa-miR-940, hsa-miR-6789-5p, hsa-miR-4484, hsa-miR-4634, hsa-miR-4745-5p, hsa-miR-4730, hsa-miR-6803-5p, hsa-miR-6798-5p, hsa-miR-3648, hsa-miR-4783-3p and hsa-miR-6836-3p can be used. Furthermore, at least one or more miRNA(s) selected from the group consisting of other liver cancer markers that can be combined with these miRNAs, i.e., hsa-miR-23b-3p, hsa-miR-23a-3p, hsa-miR-625-3p, hsa-miR-1228-3p, hsa-miR-614, hsa-miR-1913, hsa-miR-92a-2-5p, hsa-miR-187-5p, hsa-miR-16-5p, hsa-miR-92b-3p, hsa-miR-150-3p, hsa-miR-564, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-92a-3p and hsa-miR-663a can also be preferably used as a target nucleic acid. Moreover, at least one or more miRNA(s) selected from the group consisting of other liver cancer markers that can be combined with these miRNAs, i.e., hsa-miR-4688, hsa-miR-4648, hsa-miR-6085, hsa-miR-6126, hsa-miR-6880-5p, hsa-miR-328-5p, hsa-miR-6768-5p, hsa-miR-3180, hsa-miR-6087, hsa-miR-1273g-3p, hsa-miR-1225-5p, hsa-miR-3196, hsa-miR-4695-5p, hsa-miR-6732-5p, hsa-miR-638, hsa-miR-6813-5p, hsa-miR-665, hsa-miR-486-3p, hsa-miR-4466, hsa-miR-30c-1-3p, hsa-miR-3621, hsa-miR-6743-5p, hsa-miR-4298, hsa-miR-4741, hsa-miR-3619-3p, hsa-miR-6824-5p, hsa-miR-5698, hsa-miR-371a-5p, hsa-miR-4488, hsa-miR-1233-5p, hsa-miR-4723-5p, hsa-miR-24-3p, hsa-miR-1238-5p, hsa-miR-4442, hsa-miR-3928-3p, hsa-miR-6716-5p, hsa-miR-6089, hsa-miR-6124, hsa-miR-6778-5p, hsa-miR-557 and hsa-miR-6090 can also be preferably used as a target nucleic acid.

These miRNAs include, for example, a human gene comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 224 and 714 to 729 (i.e., hsa-miR-1343-3p, hsa-miR-6726-5p, hsa-miR-6515-3p, hsa-miR-4651, hsa-miR-4257, hsa-miR-3188, hsa-miR-6131, hsa-miR-6766-3p, hsa-miR-7641, hsa-miR-1249, hsa-miR-3679-3p, hsa-miR-6787-5p, hsa-miR-4454, hsa-miR-3135b, hsa-miR-6765-3p, hsa-miR-7975, hsa-miR-204-3p, hsa-miR-7977, hsa-miR-7110-5p, hsa-miR-6717-5p, hsa-miR-6870-5p, hsa-miR-663b, hsa-miR-6875-5p, hsa-miR-8072, hsa-miR-6816-5p, hsa-miR-4281, hsa-miR-6729-5p, hsa-miR-8069, hsa-miR-4706, hsa-miR-7108-5p, hsa-miR-4433b-3p, hsa-miR-6893-5p, hsa-miR-6857-5p, hsa-miR-1227-5p, hsa-miR-6741-5p, hsa-miR-451a, hsa-miR-8063, hsa-miR-3622a-5p, hsa-miR-615-5p, hsa-miR-128-1-5p, hsa-miR-6825-5p, hsa-miR-1260b, hsa-miR-4433-3p, hsa-miR-4665-5p, hsa-miR-7845-5p, hsa-miR-1908-5p, hsa-miR-6840-3p, hsa-miR-6765-5p, hsa-miR-296-5p, hsa-miR-3675-3p, hsa-miR-6781-5p, hsa-miR-423-5p, hsa-miR-

3663-3p, hsa-miR-6784-5p, hsa-miR-6749-5p, hsa-miR-1231, hsa-miR-4746-3p, hsa-miR-6780b-5p, hsa-miR-4758-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-6125, hsa-miR-6721-5p, hsa-miR-6791-5p, hsa-miR-3185, hsa-miR-1260a, hsa-miR-3197, hsa-miR-6845-5p, hsa-miR-6887-5p, hsa-miR-6738-5p, hsa-miR-6872-3p, hsa-miR-4497, hsa-miR-1229-5p, hsa-miR-6820-5p, hsa-miR-6777-5p, hsa-miR-3917, hsa-miR-5787, hsa-miR-4286, hsa-miR-6877-5p, hsa-miR-1225-3p, hsa-miR-6088, hsa-miR-6800-5p, hsa-miR-1246, hsa-miR-4467, hsa-miR-4419b, hsa-miR-1914-3p, hsa-miR-4632-5p, hsa-miR-1915-5p, hsa-miR-3940-5p, hsa-miR-1185-2-3p, hsa-miR-6746-5p, hsa-miR-5001-5p, hsa-miR-1228-5p, hsa-miR-5572, hsa-miR-4327, hsa-miR-4638-5p, hsa-miR-6799-5p, hsa-miR-6861-5p, hsa-miR-6727-5p, hsa-miR-4513, hsa-miR-6805-3p, hsa-miR-6808-5p, hsa-miR-4449, hsa-miR-1199-5p, hsa-miR-1275, hsa-miR-4792, hsa-miR-4443, hsa-miR-6891-5p, hsa-miR-6826-5p, hsa-miR-6807-5p, hsa-miR-7150, hsa-miR-4534, hsa-miR-4476, hsa-miR-4649-5p, hsa-miR-4525, hsa-miR-1915-3p, hsa-miR-4516, hsa-miR-4417, hsa-miR-642b-3p, hsa-miR-3141, hsa-miR-5100, hsa-miR-6848-5p, hsa-miR-4739, hsa-miR-4459, hsa-miR-1237-5p, hsa-miR-296-3p, hsa-miR-4665-3p, hsa-miR-6786-5p, hsa-miR-4258, hsa-miR-6510-5p, hsa-miR-1343-5p, hsa-miR-1247-3p, hsa-miR-6805-5p, hsa-miR-4492, hsa-miR-1469, hsa-miR-1268b, hsa-miR-6858-5p, hsa-miR-3937, hsa-miR-939-5p, hsa-miR-3656, hsa-miR-744-5p, hsa-miR-4687-3p, hsa-miR-4763-3p, hsa-miR-3620-5p, hsa-miR-3195, hsa-miR-6842-5p, hsa-miR-4707-5p, hsa-miR-642a-3p, hsa-miR-7113-3p, hsa-miR-4728-5p, hsa-miR-5195-3p, hsa-miR-1185-1-3p, hsa-miR-6774-5p, hsa-miR-8059, hsa-miR-3131, hsa-miR-7847-3p, hsa-miR-4463, hsa-miR-128-2-5p, hsa-miR-4508, hsa-miR-6806-5p, hsa-miR-7111-5p, hsa-miR-6782-5p, hsa-miR-4734, hsa-miR-3162-5p, hsa-miR-887-3p, hsa-miR-6752-5p, hsa-miR-6724-5p, hsa-miR-6757-5p, hsa-miR-4448, hsa-miR-671-5p, hsa-miR-3178, hsa-miR-4725-3p, hsa-miR-940, hsa-miR-6789-5p, hsa-miR-4484, hsa-miR-4634, hsa-miR-4745-5p, hsa-miR-4730, hsa-miR-6803-5p, hsa-miR-6798-5p, hsa-miR-3648, hsa-miR-4783-3p, hsa-miR-6836-3p, hsa-miR-23b-3p, hsa-miR-23a-3p, hsa-miR-625-3p, hsa-miR-1228-3p, hsa-miR-614, hsa-miR-1913, hsa-miR-92a-2-5p, hsa-miR-187-5p, hsa-miR-16-5p, hsa-miR-92b-3p, hsa-miR-150-3p, hsa-miR-564, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-92a-3p, hsa-miR-663a, hsa-miR-4688, hsa-miR-4648, hsa-miR-6085, hsa-miR-6126, hsa-miR-6880-5p, hsa-miR-328-5p, hsa-miR-6768-5p, hsa-miR-3180, hsa-miR-6087, hsa-miR-1273g-3p, hsa-miR-1225-5p, hsa-miR-3196, hsa-miR-4695-5p, hsa-miR-6732-5p, hsa-miR-638, hsa-miR-6813-5p, hsa-miR-665, hsa-miR-486-3p, hsa-miR-4466, hsa-miR-30c-1-3p, hsa-miR-3621, hsa-miR-6743-5p, hsa-miR-4298, hsa-miR-4741, hsa-miR-3619-3p, hsa-miR-6824-5p, hsa-miR-5698, hsa-miR-371a-5p, hsa-miR-4488, hsa-miR-1233-5p, hsa-miR-4723-5p, hsa-miR-24-3p, hsa-miR-1238-5p, hsa-miR-4442, hsa-miR-3928-3p, hsa-miR-6716-5p, hsa-miR-6089, hsa-miR-6124, hsa-miR-6778-5p, hsa-miR-557 and hsa-miR-6090, respectively), a congener thereof, a transcript thereof, or/and a variant or a derivative thereof. In this context, the gene, the congener, the transcript, the variant, and the derivative are as defined above.

The target nucleic acid is preferably a human gene comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 765 or a transcript thereof, more preferably the transcript, i.e., a miRNA or its precursor RNA (pri-miRNA or pre-miRNA).

The first target gene is the hsa-miR-1343-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The second target gene is the hsa-miR-6726-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The third target gene is the hsa-miR-6515-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The fourth target gene is the hsa-miR-4651 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The fifth target gene is the hsa-miR-4257 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The sixth target gene is the hsa-miR-3188 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The seventh target gene is the hsa-miR-6131 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The eighth target gene is the hsa-miR-6766-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The ninth target gene is the hsa-miR-7641 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 10th target gene is the hsa-miR-1249 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 11th target gene is the hsa-miR-3679-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 12th target gene is the hsa-miR-6787-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 13th target gene is the hsa-miR-4454 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 14th target gene is the hsa-miR-3135b gene, a congener thereof, a transcript thereof, or a variant or a derivative

thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 15th target gene is the hsa-miR-6765-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 16th target gene is the hsa-miR-7975 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 17th target gene is the hsa-miR-204-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 18th target gene is the hsa-miR-7977 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 19th target gene is the hsa-miR-7110-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 20th target gene is the hsa-miR-6717-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 21st target gene is the hsa-miR-6870-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 22nd target gene is the hsa-miR-663b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 23rd target gene is the hsa-miR-6875-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 24th target gene is the hsa-miR-8072 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 25th target gene is the hsa-miR-6816-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 26th target gene is the hsa-miR-4281 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 27th target gene is the hsa-miR-6729-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 28th target gene is the hsa-miR-8069 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 29th target gene is the hsa-miR-4706 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 30th target gene is the hsa-miR-7108-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 31st target gene is the hsa-miR-4433b-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 32nd target gene is the hsa-miR-6893-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 33rd target gene is the hsa-miR-6857-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 34th target gene is the hsa-miR-1227-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 35th target gene is the hsa-miR-6741-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 36th target gene is the hsa-miR-451a gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 37th target gene is the hsa-miR-8063 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 38th target gene is the hsa-miR-3622a-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 39th target gene is the hsa-miR-615-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 40th target gene is the hsa-miR-128-1-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 41st target gene is the hsa-miR-6825-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 42nd target gene is the hsa-miR-1260b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 43rd target gene is the hsa-miR-4433-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 44th target gene is the hsa-miR-4665-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 45th target gene is the hsa-miR-7845-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 46th target gene is the hsa-miR-1908-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 47th target gene is the hsa-miR-6840-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 48th target gene is the hsa-miR-6765-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 49th target gene is the hsa-miR-296-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 50th target gene is the hsa-miR-3675-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 51st target gene is the hsa-miR-6781-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 52nd target gene is the hsa-miR-423-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 53rd target gene is the hsa-miR-3663-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 54th target gene is the hsa-miR-6784-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 55th target gene is the hsa-miR-6749-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 56th target gene is the hsa-miR-1231 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 57th target gene is the hsa-miR-4746-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 58th target gene is the hsa-miR-6780b-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 59th target gene is the hsa-miR-4758-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 60th target gene is the hsa-miR-3679-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 61st target gene is the hsa-miR-3184-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 62nd target gene is the hsa-miR-6125 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 63rd target gene is the hsa-miR-6721-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 64th target gene is the hsa-miR-6791-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 65th target gene is the hsa-miR-3185 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 66th target gene is the hsa-miR-1260a gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 67th target gene is the hsa-miR-3197 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that

change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 68th target gene is the hsa-miR-6845-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 69th target gene is the hsa-miR-6887-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 70th target gene is the hsa-miR-6738-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 71st target gene is the hsa-miR-6872-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 72nd target gene is the hsa-miR-4497 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 73rd target gene is the hsa-miR-1229-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 74th target gene is the hsa-miR-6820-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 75th target gene is the hsa-miR-6777-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 76th target gene is the hsa-miR-3917 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 77th target gene is the hsa-miR-5787 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 78th target gene is the hsa-miR-4286 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 79th target gene is the hsa-miR-6877-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 80th target gene is the hsa-miR-1225-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 81st target gene is the hsa-miR-6088 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 82nd target gene is the hsa-miR-6800-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 83rd target gene is the hsa-miR-1246 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 84th target gene is the hsa-miR-4467 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 85th target gene is the hsa-miR-4419b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 86th target gene is the hsa-miR-1914-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 87th target gene is the hsa-miR-4632-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 88th target gene is the hsa-miR-1915-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 89th target gene is the hsa-miR-3940-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 90th target gene is the hsa-miR-1185-2-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 91st target gene is the hsa-miR-6746-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 92nd target gene is the hsa-miR-5001-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 93rd target gene is the hsa-miR-1228-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 94th target gene is the hsa-miR-5572 gene, a congener thereof, a transcript thereof, or a variant or a derivative

thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 95th target gene is the hsa-miR-4327 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 96th target gene is the hsa-miR-4638-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 97th target gene is the hsa-miR-6799-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 98th target gene is the hsa-miR-6861-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 99th target gene is the hsa-miR-6727-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 100th target gene is the hsa-miR-4513 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 101st target gene is the hsa-miR-6805-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 102nd target gene is the hsa-miR-6808-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 103rd target gene is the hsa-miR-4449 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 104th target gene is the hsa-miR-1199-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 105th target gene is the hsa-miR-1275 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 106th target gene is the hsa-miR-4792 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 107th target gene is the hsa-miR-4443 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 108th target gene is the hsa-miR-6891-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 109th target gene is the hsa-miR-6826-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 110th target gene is the hsa-miR-6807-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 111th target gene is the hsa-miR-7150 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 112th target gene is the hsa-miR-4534 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 113th target gene is the hsa-miR-4476 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 114th target gene is the hsa-miR-4649-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 115th target gene is the hsa-miR-4525 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 116th target gene is the hsa-miR-1915-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 117th target gene is the hsa-miR-4516 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 118th target gene is the hsa-miR-4417 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 119th target gene is the hsa-miR-642b-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 120th target gene is the hsa-miR-3141 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 121st target gene is the hsa-miR-5100 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 122nd target gene is the hsa-miR-6848-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 123rd target gene is the hsa-miR-4739 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 124th target gene is the hsa-miR-4459 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 125th target gene is the hsa-miR-1237-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 126th target gene is the hsa-miR-296-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 127th target gene is the hsa-miR-4665-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 128th target gene is the hsa-miR-6786-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 129th target gene is the hsa-miR-4258 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 130th target gene is the hsa-miR-6510-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 131st target gene is the hsa-miR-1343-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 132nd target gene is the hsa-miR-1247-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 133rd target gene is the hsa-miR-6805-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 134th target gene is the hsa-miR-4492 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 135th target gene is the hsa-miR-1469 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 136th target gene is the hsa-miR-1268b gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 137th target gene is the hsa-miR-6858-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 138th target gene is the hsa-miR-3937 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 139th target gene is the hsa-miR-939-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 140th target gene is the hsa-miR-3656 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 141st target gene is the hsa-miR-744-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 142nd target gene is the hsa-miR-4687-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 143rd target gene is the hsa-miR-4763-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 144th target gene is the hsa-miR-3620-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 145th target gene is the hsa-miR-3195 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 146th target gene is the hsa-miR-6842-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 147th target gene is the hsa-miR-4707-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports

show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 148th target gene is the hsa-miR-642a-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 149th target gene is the hsa-miR-7113-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 150th target gene is the hsa-miR-4728-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 151st target gene is the hsa-miR-5195-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 152nd target gene is the hsa-miR-1185-1-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 153rd target gene is the hsa-miR-6774-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 154th target gene is the hsa-miR-8059 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 155th target gene is the hsa-miR-3131 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 156th target gene is the hsa-miR-7847-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 157th target gene is the hsa-miR-4463 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 158th target gene is the hsa-miR-128-2-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 159th target gene is the hsa-miR-4508 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 160th target gene is the hsa-miR-6806-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 161st target gene is the hsa-miR-7111-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 162nd target gene is the hsa-miR-6782-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 163rd target gene is the hsa-miR-4734 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 164th target gene is the hsa-miR-3162-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 165th target gene is the hsa-miR-887-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 166th target gene is the hsa-miR-6752-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 167th target gene is the hsa-miR-6724-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 168th target gene is the hsa-miR-23b-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literatures 2 and 3).

The 169th target gene is the hsa-miR-23a-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 2).

The 170th target gene is the hsa-miR-625-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 4).

The 171st target gene is the hsa-miR-1228-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 172nd target gene is the hsa-miR-614 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 2).

The 173rd target gene is the hsa-miR-1913 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 4).

The 174th target gene is the hsa-miR-92a-2-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 1).

The 175th target gene is the hsa-miR-187-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 5).

The 176th target gene is the hsa-miR-16-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literatures 4 and 5).

The 177th target gene is the hsa-miR-92b-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 1).

The 178th target gene is the hsa-miR-150-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 2).

The 179th target gene is the hsa-miR-564 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 2).

The 180th target gene is the hsa-miR-125a-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 3).

The 181st target gene is the hsa-miR-92b-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 1).

The 182nd target gene is the hsa-miR-92a-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literatures 1, 4, and 5).

The 183rd target gene is the hsa-miR-663a gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 4).

The 184th target gene is the hsa-miR-4688 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 185th target gene is the hsa-miR-4648 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 186th target gene is the hsa-miR-6085 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 187th target gene is the hsa-miR-6126 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 188th target gene is the hsa-miR-6880-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 189th target gene is the hsa-miR-328-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 190th target gene is the hsa-miR-6768-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 191st target gene is the hsa-miR-3180 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 192nd target gene is the hsa-miR-6087 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 193rd target gene is the hsa-miR-1273g-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 194th target gene is the hsa-miR-1225-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 195th target gene is the hsa-miR-3196 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 196th target gene is the hsa-miR-4695-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 197th target gene is the hsa-miR-6732-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 198th target gene is the hsa-miR-638 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 199th target gene is the hsa-miR-6813-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 200th target gene is the hsa-miR-665 gene, a congener thereof, a transcript thereof, or a variant or a derivative

thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 201st target gene is the hsa-miR-486-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literatures 2 and 3).

The 202nd target gene is the hsa-miR-4466 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 203rd target gene is the hsa-miR-30c-1-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literatures 3 and 5).

The 204th target gene is the hsa-miR-3621 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 205th target gene is the hsa-miR-6743-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 206th target gene is the hsa-miR-4298 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 207th target gene is the hsa-miR-4741 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 208th target gene is the hsa-miR-3619-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 209th target gene is the hsa-miR-6824-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 210th target gene is the hsa-miR-5698 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 211th target gene is the hsa-miR-371a-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 212th target gene is the hsa-miR-4488 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 213th target gene is the hsa-miR-1233-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 214th target gene is the hsa-miR-4723-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 215th target gene is the hsa-miR-24-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 2).

The 216th target gene is the hsa-miR-1238-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 217th target gene is the hsa-miR-4442 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 218th target gene is the hsa-miR-3928-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 219th target gene is the hsa-miR-6716-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 220th target gene is the hsa-miR-6089 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 221st target gene is the hsa-miR-6124 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 222nd target gene is the hsa-miR-6778-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 223rd target gene is the hsa-miR-557 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. The previously known report shows that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer (Patent Literature 2).

The 224th target gene is the hsa-miR-6090 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 225th target gene is the hsa-miR-6757-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 226th target gene is the hsa-miR-4448 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that

change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 227th target gene is the hsa-miR-671-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 228th target gene is the hsa-miR-3178 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 229th target gene is the hsa-miR-4725-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 230th target gene is the hsa-miR-940 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 231st target gene is the hsa-miR-6789-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 232nd target gene is the hsa-miR-4484 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 233rd target gene is the hsa-miR-4634 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 234th target gene is the hsa-miR-4745-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 235th target gene is the hsa-miR-4730 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 236th target gene is the hsa-miR-6803-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 237th target gene is the hsa-miR-6798-5p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 238th target gene is the hsa-miR-3648 gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 239th target gene is the hsa-miR-4783-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

The 240th target gene is the hsa-miR-6836-3p gene, a congener thereof, a transcript thereof, or a variant or a derivative thereof. None of the previously known reports show that change in the expression of the gene or the transcript thereof can serve as a marker for liver cancer.

2. Nucleic Acid Probe or Primer for Detection of Liver Cancer

In the present invention, a nucleic acid capable of specifically binding to any of the target nucleic acids as the liver cancer markers described above can be used as a nucleic acid, for example, a nucleic acid probe or a primer, for the detection or diagnosis of liver cancer.

In the present invention, the nucleic acid probe or the primer that can be used for detecting liver cancer or for diagnosing liver cancer enables qualitative and/or quantitative measurement of the presence, expression level, or abundance of a target nucleic acid as the liver cancer marker described above, for example, human-derived hsa-miR-1343-3p, hsa-miR-6726-5p, hsa-miR-6515-3p, hsa-miR-4651, hsa-miR-4257, hsa-miR-3188, hsa-miR-6131, hsa-miR-6766-3p, hsa-miR-7641, hsa-miR-1249, hsa-miR-3679-3p, hsa-miR-6787-5p, hsa-miR-4454, hsa-miR-3135b, hsa-miR-6765-3p, hsa-miR-7975, hsa-miR-204-3p, hsa-miR-7977, hsa-miR-7110-5p, hsa-miR-6717-5p, hsa-miR-6870-5p, hsa-miR-663b, hsa-miR-6875-5p, hsa-miR-8072, hsa-miR-6816-5p, hsa-miR-4281, hsa-miR-6729-5p, hsa-miR-8069, hsa-miR-4706, hsa-miR-7108-5p, hsa-miR-4433b-3p, hsa-miR-6893-5p, hsa-miR-6857-5p, hsa-miR-1227-5p, hsa-miR-6741-5p, hsa-miR-451a, hsa-miR-8063, hsa-miR-3622a-5p, hsa-miR-615-5p, hsa-miR-128-1-5p, hsa-miR-6825-5p, hsa-miR-1260b, hsa-miR-4433-3p, hsa-miR-4665-5p, hsa-miR-7845-5p, hsa-miR-1908-5p, hsa-miR-6840-3p, hsa-miR-6765-5p, hsa-miR-296-5p, hsa-miR-3675-3p, hsa-miR-6781-5p, hsa-miR-423-5p, hsa-miR-3663-3p, hsa-miR-6784-5p, hsa-miR-6749-5p, hsa-miR-1231, hsa-miR-4746-3p, hsa-miR-6780b-5p, hsa-miR-4758-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-6125, hsa-miR-6721-5p, hsa-miR-6791-5p, hsa-miR-3185, hsa-miR-1260a, hsa-miR-3197, hsa-miR-6845-5p, hsa-miR-6887-5p, hsa-miR-6738-5p, hsa-miR-6872-3p, hsa-miR-4497, hsa-miR-1229-5p, hsa-miR-6820-5p, hsa-miR-6777-5p, hsa-miR-3917, hsa-miR-5787, hsa-miR-4286, hsa-miR-6877-5p, hsa-miR-1225-3p, hsa-miR-6088, hsa-miR-6800-5p, hsa-miR-1246, hsa-miR-4467, hsa-miR-4419b, hsa-miR-1914-3p, hsa-miR-4632-5p, hsa-miR-1915-5p, hsa-miR-3940-5p, hsa-miR-1185-2-3p, hsa-miR-6746-5p, hsa-miR-5001-5p, hsa-miR-1228-5p, hsa-miR-5572, hsa-miR-4327, hsa-miR-4638-5p, hsa-miR-6799-5p, hsa-miR-6861-5p, hsa-miR-6727-5p, hsa-miR-4513, hsa-miR-6805-3p, hsa-miR-6808-5p, hsa-miR-4449, hsa-miR-1199-5p, hsa-miR-1275, hsa-miR-4792, hsa-miR-4443, hsa-miR-6891-5p, hsa-miR-6826-5p, hsa-miR-6807-5p, hsa-miR-7150, hsa-miR-4534, hsa-miR-4476, hsa-miR-4649-5p, hsa-miR-4525, hsa-miR-1915-3p, hsa-miR-4516, hsa-miR-4417, hsa-miR-642b-3p, hsa-miR-3141, hsa-miR-5100, hsa-miR-6848-5p, hsa-miR-4739, hsa-miR-4459, hsa-miR-1237-5p, hsa-miR-296-3p, hsa-miR-4665-3p, hsa-miR-6786-5p, hsa-miR-4258, hsa-miR-6510-5p, hsa-miR-1343-5p, hsa-miR-1247-3p, hsa-miR-6805-5p, hsa-miR-4492, hsa-miR-1469, hsa-miR-1268b, hsa-miR-6858-5p, hsa-miR-3937, hsa-miR-939-5p, hsa-miR-3656, hsa-miR-744-5p, hsa-miR-4687-3p, hsa-miR-4763-3p, hsa-miR-3620-5p, hsa-miR-3195, hsa-miR-6842-5p, hsa-miR-4707-5p, hsa-miR-642a-3p, hsa-miR-7113-3p, hsa-miR-4728-5p, hsa-miR-5195-3p, hsa-miR-1185-1-3p, hsa-miR-6774-5p, hsa-miR-8059, hsa-miR-3131, hsa-miR-7847-3p, hsa-miR-4463, hsa-miR-128-2-5p, hsa-miR-4508, hsa-miR-6806-5p,

hsa-miR-7111-5p, hsa-miR-6782-5p, hsa-miR-4734, hsa-miR-3162-5p, hsa-miR-887-3p, hsa-miR-6752-5p, hsa-miR-6724-5p, hsa-miR-6757-5p, hsa-miR-4448, hsa-miR-671-5p, hsa-miR-3178, hsa-miR-4725-3p, hsa-miR-940, hsa-miR-6789-5p, hsa-miR-4484, hsa-miR-4634, hsa-miR-4745-5p, hsa-miR-4730, hsa-miR-6803-5p, hsa-miR-6798-5p, hsa-miR-3648, hsa-miR-4783-3p, or hsa-miR-6836-3p, or a combination thereof, or a congener thereof, a transcript thereof, or a variant or derivative thereof; and, optionally in combination therewith, hsa-miR-23b-3p, hsa-miR-23a-3p, hsa-miR-625-3p, hsa-miR-1228-3p, hsa-miR-614, hsa-miR-1913, hsa-miR-92a-2-5p, hsa-miR-187-5p, hsa-miR-16-5p, hsa-miR-92b-3p, hsa-miR-150-3p, hsa-miR-564, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-92a-3p, or hsa-miR-663a, or a combination thereof, a congener thereof, a transcript thereof, or a variant or derivative thereof; and optionally in combination therewith, hsa-miR-4688, hsa-miR-4648, hsa-miR-6085, hsa-miR-6126, hsa-miR-6880-5p, hsa-miR-328-5p, hsa-miR-6768-5p, hsa-miR-3180, hsa-miR-6087, hsa-miR-1273g-3p, hsa-miR-1225-5p, hsa-miR-3196, hsa-miR-4695-5p, hsa-miR-6732-5p, hsa-miR-638, hsa-miR-6813-5p, hsa-miR-665, hsa-miR-486-3p, hsa-miR-4466, hsa-miR-30c-1-3p, hsa-miR-3621, hsa-miR-6743-5p, hsa-miR-4298, hsa-miR-4741, hsa-miR-3619-3p, hsa-miR-6824-5p, hsa-miR-5698, hsa-miR-371a-5p, hsa-miR-4488, hsa-miR-1233-5p, hsa-miR-4723-5p, hsa-miR-24-3p, hsa-miR-1238-5p, hsa-miR-4442, hsa-miR-3928-3p, hsa-miR-6716-5p, hsa-miR-6089, hsa-miR-6124, hsa-miR-6778-5p, hsa-miR-557, and hsa-miR-6090, or a combination thereof, a congener thereof, a transcript thereof, or a variant or derivative thereof.

The expression level of each target nucleic acid described above is increased or decreased (hereinafter, referred to as "increased/decreased") depending on the type of the target nucleic acid in a subject having liver cancer as compared with a healthy subject. Hence, the nucleic acid of the present invention can be effectively used for measuring the expression level of the target nucleic acid described above in a body fluid derived from a subject (e.g., a human) suspected of having liver cancer and a body fluid derived from a healthy subject and comparing them to detect liver cancer.

The nucleic acid probe or the primer that can be used in the present invention is a nucleic acid probe capable of specifically binding to a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 1 to 167 and 714 to 729, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 1 to 167 and 714 to 729.

The nucleic acid probe or the primer that can be further used in the present invention may comprise a nucleic acid probe capable of specifically binding to a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 168 to 183, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 168 to 183.

The nucleic acid probe or the primer that can be further used in the present invention may comprise a nucleic acid probe capable of specifically binding to a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 184 to 224, or a primer for amplifying a polynucleotide consisting of a nucleotide sequence represented by at least one of SEQ ID NOs: 184 to 224.

Specifically, these nucleic acid probes or primers comprise a combination of one or more polynucleotides selected from a group of polynucleotides comprising nucleotide sequences represented by any of SEQ ID NOs: 1 to 765 or nucleotide sequences derived from the nucleotide sequences by the replacement of u with t, and a group of complementary polynucleotides thereof, a group of polynucleotides respectively hybridizing under stringent conditions (mentioned later) to DNAs consisting of nucleotide sequences complementary to these nucleotide sequences, and a group of complementary polynucleotides thereof, and a group of polynucleotides comprising 15 or more, preferably 17 or more consecutive nucleotides in the nucleotide sequences of these polynucleotide groups. These polynucleotides can be used as nucleic acid probes and primers for detecting the liver cancer markers as target nucleic acids.

More specifically, examples of the nucleic acid probe or the primer that can be used in the present invention include one or more polynucleotide(s) selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(b) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729,

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

In addition to at least one or more polynucleotide(s) selected from the group consisting of the polynucleotides (a) to (e), the nucleic acid probe or the primer that can be further used in the present invention may comprise a polynucleotide selected from the group consisting of the following polynucleotides (f) to (j):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183,

(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i).

In addition to at least one or more polynucleotide(s) selected from the group consisting of the polynucleotides (a)

to (j), the nucleic acid probe or the primer that can be further used in the present invention may comprise a polynucleotide selected from the group consisting of the following polynucleotides (k) to (o):

(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224,

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

For these polynucleotides, the "fragment thereof comprising 15 or more consecutive nucleotides" can comprise the number of nucleotides in the range from, for example, 15 consecutive nucleotides to less than the total number of nucleotides of the sequence, 17 consecutive nucleotides to less than the total number of nucleotides of the sequence, or 19 consecutive nucleotides to less than the total number of nucleotides of the sequence, in the nucleotide sequence of each polynucleotide, though the fragment is not limited thereto.

These polynucleotides or fragments thereof used in the present invention may each be DNA or may each be RNA.

The polynucleotides that can be used in the present invention can each be prepared by use of a general technique such as a DNA recombination technique, PCR, or a method using an automatic DNA/RNA synthesizer.

The DNA recombination technique and the PCR can employ a technique described in, for example, Ausubel et al., Current Protocols in Molecular Biology, John Willey & Sons, US (1993); and Sambrook et al., Molecular Cloning—A Laboratory Manual, Cold Spring Harbor Laboratory Press, US (1989).

The human-derived hsa-miR-1343-3p, hsa-miR-6726-5p, hsa-miR-6515-3p, hsa-miR-4651, hsa-miR-4257, hsa-miR-3188, hsa-miR-6131, hsa-miR-6766-3p, hsa-miR-7641, hsa-miR-1249, hsa-miR-3679-3p, hsa-miR-6787-5p, hsa-miR-4454, hsa-miR-3135b, hsa-miR-6765-3p, hsa-miR-7975, hsa-miR-204-3p, hsa-miR-7977, hsa-miR-7110-5p, hsa-miR-6717-5p, hsa-miR-6870-5p, hsa-miR-663b, hsa-miR-6875-5p, hsa-miR-8072, hsa-miR-6816-5p, hsa-miR-4281, hsa-miR-6729-5p, hsa-miR-8069, hsa-miR-4706, hsa-miR-7108-5p, hsa-miR-4433b-3p, hsa-miR-6893-5p, hsa-miR-6857-5p, hsa-miR-1227-5p, hsa-miR-6741-5p, hsa-miR-451a, hsa-miR-8063, hsa-miR-3622a-5p, hsa-miR-615-5p, hsa-miR-128-1-5p, hsa-miR-6825-5p, hsa-miR-1260b, hsa-miR-4433-3p, hsa-miR-4665-5p, hsa-miR-7845-5p, hsa-miR-1908-5p, hsa-miR-6840-3p, hsa-miR-6765-5p, hsa-miR-296-5p, hsa-miR-3675-3p, hsa-miR-6781-5p, hsa-miR-423-5p, hsa-miR-3663-3p, hsa-miR-6784-5p, hsa-miR-6749-5p, hsa-miR-1231, hsa-miR-4746-3p, hsa-miR-6780b-5p, hsa-miR-4758-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-6125, hsa-miR-6721-5p, hsa-miR-6791-5p, hsa-miR-3185, hsa-miR-1260a, hsa-miR-3197, hsa-miR-6845-5p, hsa-miR-6887-5p, hsa-miR-6738-5p, hsa-miR-6872-3p, hsa-miR-4497, hsa-miR-1229-5p, hsa-miR-6820-5p, hsa-miR-6777-5p, hsa-miR-3917, hsa-miR-5787, hsa-miR-4286, hsa-miR-6877-5p, hsa-miR-1225-3p, hsa-miR-6088, hsa-miR-6800-5p, hsa-miR-1246, hsa-miR-4467, hsa-miR-4419b, hsa-miR-1914-3p, hsa-miR-4632-5p, hsa-miR-1915-5p, hsa-miR-3940-5p, hsa-miR-1185-2-3p, hsa-miR-6746-5p, hsa-miR-5001-5p, hsa-miR-1228-5p, hsa-miR-5572, hsa-miR-4327, hsa-miR-4638-5p, hsa-miR-6799-5p, hsa-miR-6861-5p, hsa-miR-6727-5p, hsa-miR-4513, hsa-miR-6805-3p, hsa-miR-6808-5p, hsa-miR-4449, hsa-miR-1199-5p, hsa-miR-1275, hsa-miR-4792, hsa-miR-4443, hsa-miR-6891-5p, hsa-miR-6826-5p, hsa-miR-6807-5p, hsa-miR-7150, hsa-miR-4534, hsa-miR-4476, hsa-miR-4649-5p, hsa-miR-4525, hsa-miR-1915-3p, hsa-miR-4516, hsa-miR-4417, hsa-miR-642b-3p, hsa-miR-3141, hsa-miR-5100, hsa-miR-6848-5p, hsa-miR-4739, hsa-miR-4459, hsa-miR-1237-5p, hsa-miR-296-3p, hsa-miR-4665-3p, hsa-miR-6786-5p, hsa-miR-4258, hsa-miR-6510-5p, hsa-miR-1343-5p, hsa-miR-1247-3p, hsa-miR-6805-5p, hsa-miR-4492, hsa-miR-1469, hsa-miR-1268b, hsa-miR-6858-5p, hsa-miR-3937, hsa-miR-939-5p, hsa-miR-3656, hsa-miR-744-5p, hsa-miR-4687-3p, hsa-miR-4763-3p, hsa-miR-3620-5p, hsa-miR-3195, hsa-miR-6842-5p, hsa-miR-4707-5p, hsa-miR-642a-3p, hsa-miR-7113-3p, hsa-miR-4728-5p, hsa-miR-5195-3p, hsa-miR-1185-1-3p, hsa-miR-6774-5p, hsa-miR-8059, hsa-miR-3131, hsa-miR-7847-3p, hsa-miR-4463, hsa-miR-128-2-5p, hsa-miR-4508, hsa-miR-6806-5p, hsa-miR-7111-5p, hsa-miR-6782-5p, hsa-miR-4734, hsa-miR-3162-5p, hsa-miR-887-3p, hsa-miR-6752-5p, hsa-miR-6724-5p, hsa-miR-6757-5p, hsa-miR-4448, hsa-miR-671-5p, hsa-miR-3178, hsa-miR-4725-3p, hsa-miR-940, hsa-miR-6789-5p, hsa-miR-4484, hsa-miR-4634, hsa-miR-4745-5p, hsa-miR-4730, hsa-miR-6803-5p, hsa-miR-6798-5p, hsa-miR-3648, hsa-miR-4783-3p, hsa-miR-6836-3p, hsa-miR-23b-3p, hsa-miR-23a-3p, hsa-miR-625-3p, hsa-miR-1228-3p, hsa-miR-614, hsa-miR-1913, hsa-miR-92a-2-5p, hsa-miR-187-5p, hsa-miR-16-5p, hsa-miR-92b-3p, hsa-miR-150-3p, hsa-miR-564, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-92a-3p, hsa-miR-663a, hsa-miR-4688, hsa-miR-4648, hsa-miR-6085, hsa-miR-6126, hsa-miR-6880-5p, hsa-miR-328-5p, hsa-miR-6768-5p, hsa-miR-3180, hsa-miR-6087, hsa-miR-1273g-3p, hsa-miR-1225-5p, hsa-miR-3196, hsa-miR-4695-5p, hsa-miR-6732-5p, hsa-miR-638, hsa-miR-6813-5p, hsa-miR-665, hsa-miR-486-3p, hsa-miR-4466, hsa-miR-30c-1-3p, hsa-miR-3621, hsa-miR-6743-5p, hsa-miR-4298, hsa-miR-4741, hsa-miR-3619-3p, hsa-miR-6824-5p, hsa-miR-5698, hsa-miR-371a-5p, hsa-miR-4488, hsa-miR-1233-5p, hsa-miR-4723-5p, hsa-miR-24-3p, hsa-miR-1238-5p, hsa-miR-4442, hsa-miR-3928-3p, hsa-miR-6716-5p, hsa-miR-6089, hsa-miR-6124, hsa-miR-6778-5p, hsa-miR-557 and hsa-miR-6090 represented by SEQ ID NOs: 1 to 224 and 714 to 729 are known in the art, and their obtainment methods are also known as mentioned above. Therefore, each polynucleotide that can be used as a nucleic acid probe or a primer in the present invention can be prepared by cloning the gene.

Such a nucleic acid probe or a primer can be chemically synthesized using an automated DNA synthesizer. In general, a phosphoramidite method is used in this synthesis, and single-stranded DNA up to approximately 100 nucleotides can be automatically synthesized by this method. The automated DNA synthesizer is commercially available from, for example, Polygen GmbH, ABI, or Applied Biosystems, Inc.

Alternatively, the polynucleotide of the present invention can also be prepared by a cDNA cloning method. The cDNA cloning technique can employ, for example, microRNA Cloning Kit Wako.

In this context, the sequences of the nucleic acid probe and the primer for detecting the polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 224 and 714 to 729 do not exist as miRNAs or precursors thereof in vivo. For example, the nucleotide sequences represented by SEQ ID NO: 1 and SEQ ID NO: 131 are produced from the precursor represented by SEQ ID NO: 225. This precursor has a hairpin-like structure as shown in FIG. **1**, and the nucleotide sequences represented by SEQ ID NO: 1 and SEQ ID NO: 131 have mismatch sequences with each other. Therefore, a nucleotide sequence completely complementary to the nucleotide sequence represented by SEQ ID NO: 1 or SEQ ID NO: 131 is not naturally produced in vivo. Likewise, the nucleic acid probe and the primer for detecting the nucleotide sequence represented by any of SEQ ID NOs: 1 to 224 and 714 to 729 each have an artificial nucleotide sequence that does not exist in vivo.

3. Kit or Device for Detection of Liver Cancer

The present invention also provides a kit or a device for the detection of liver cancer, comprising one or more polynucleotide(s) (which may include a variant, a fragment, or a derivative thereof; hereinafter, also referred to as a polynucleotide for detection) that can be used as a nucleic acid probe or a primer in the present invention for measuring a target nucleic acid as a liver cancer marker.

The target nucleic acid as a liver cancer marker according to the present invention is preferably selected from the following group 1:

miR-1343-3p, miR-6726-5p, miR-6515-3p, miR-4651, miR-4257, miR-3188, miR-6131, miR-6766-3p, miR-7641, miR-1249, miR-3679-3p, miR-6787-5p, miR-4454, miR-3135b, miR-6765-3p, miR-7975, miR-204-3p, miR-7977, miR-7110-5p, miR-6717-5p, miR-6870-5p, miR-663b, miR-6875-5p, miR-8072, miR-6816-5p, miR-4281, miR-6729-5p, miR-8069, miR-4706, miR-7108-5p, miR-4433b-3p, miR-6893-5p, miR-6857-5p, miR-1227-5p, miR-6741-5p, miR-451a, miR-8063, miR-3622a-5p, miR-615-5p, miR-128-1-5p, miR-6825-5p, miR-1260b, miR-4433-3p, miR-4665-5p, miR-7845-5p, miR-1908-5p, miR-6840-3p, miR-6765-5p, miR-296-5p, miR-3675-3p, miR-6781-5p, miR-423-5p, miR-3663-3p, miR-6784-5p, miR-6749-5p, miR-1231, miR-4746-3p, miR-6780b-5p, miR-4758-5p, miR-3679-5p, miR-3184-5p, miR-6125, miR-6721-5p, miR-6791-5p, miR-3185, miR-1260a, miR-3197, miR-6845-5p, miR-6887-5p, miR-6738-5p, miR-6872-3p, miR-4497, miR-1229-5p, miR-6820-5p, miR-6777-5p, miR-3917, miR-5787, miR-4286, miR-6877-5p, miR-1225-3p, miR-6088, miR-6800-5p, miR-1246, miR-4467, miR-4419b, miR-1914-3p, miR-4632-5p, miR-1915-5p, miR-3940-5p, miR-1185-2-3p, miR-6746-5p, miR-5001-5p, miR-1228-5p, miR-5572, miR-4327, miR-4638-5p, miR-6799-5p, miR-6861-5p, miR-6727-5p, miR-4513, miR-6805-3p, miR-6808-5p, miR-4449, miR-1199-5p, miR-1275, miR-4792, miR-4443, miR-6891-5p, miR-6826-5p, miR-6807-5p, miR-7150, miR-4534, miR-4476, miR-4649-5p, miR-4525, miR-1915-3p, miR-4516, miR-4417, miR-642b-3p, miR-3141, miR-5100, miR-6848-5p, miR-4739, miR-4459, miR-1237-5p, miR-296-3p, miR-4665-3p, miR-6786-5p, miR-4258, miR-6510-5p, miR-1343-5p, miR-1247-3p, miR-6805-5p, miR-4492, miR-1469, miR-1268b, miR-6858-5p, miR-3937, miR-939-5p, miR-3656, miR-744-5p, miR-4687-3p, miR-4763-3p, miR-3620-5p, miR-3195, miR-6842-5p, miR-4707-5p, miR-642a-3p, miR-7113-3p, miR-4728-5p, miR-5195-3p, miR-1185-1-3p, miR-6774-5p, miR-8059, miR-3131, miR-7847-3p, miR-4463, miR-128-2-5p, miR-4508, miR-6806-5p, miR-7111-5p, miR-6782-5p, miR-4734, miR-3162-5p, miR-887-3p, miR-6752-5p, miR-6724-5p, miR-6757-5p, miR-4448, miR-671-5p, miR-3178, miR-4725-3p, miR-940, miR-6789-5p, miR-4484, miR-4634, miR-4745-5p, miR-4730, miR-6803-5p, miR-6798-5p, miR-3648, miR-4783-3p and miR-6836-3p.

An additional target nucleic acid that may be optionally used in the measurement is preferably selected from the following group 2: miR-23b-3p, miR-23a-3p, miR-625-3p, miR-1228-3p, miR-614, miR-1913, miR-92a-2-5p, miR-187-5p, miR-16-5p, miR-92b-3p, miR-150-3p, miR-564, miR-125a-3p, miR-92b-5p, miR-92a-3p and miR-663a.

An additional target nucleic acid that can be optionally further used in the measurement is preferably selected from the following group 3: miR-4688, miR-4648, miR-6085, miR-6126, miR-6880-5p, miR-328-5p, miR-6768-5p, miR-3180, miR-6087, miR-1273g-3p, miR-1225-5p, miR-3196, miR-4695-5p, miR-6732-5p, miR-638, miR-6813-5p, miR-665, miR-486-3p, miR-4466, miR-30c-1-3p, miR-3621, miR-6743-5p, miR-4298, miR-4741, miR-3619-3p, miR-6824-5p, miR-5698, miR-371a-5p, miR-4488, miR-1233-5p, miR-4723-5p, miR-24-3p, miR-1238-5p, miR-4442, miR-3928-3p, miR-6716-5p, miR-6089, miR-6124, miR-6778-5p, miR-557 and miR-6090.

The kit or the device of the present invention comprises a nucleic acid capable of specifically binding to any of the target nucleic acids as the liver cancer markers described above, preferably one or more polynucleotide(s) selected from the nucleic acid probes or the primers described in Section 2 above, specifically, the polynucleotides described in Section 2 above, or variant(s) thereof.

Specifically, the kit or the device of the present invention may comprise at least one or more polynucleotide(s) comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, polynucleotide(s) comprising (or consisting of) a complementary sequence thereof, polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, or variant(s) or fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

The kit or the device of the present invention may further comprise one or more polynucleotide(s) comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, polynucleotide(s) comprising (or consisting of) a complementary sequence thereof, polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, variant(s) or fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

The kit or the device of the present invention may further comprise one or more polynucleotide(s) comprising (or consisting of) a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, polynucleotide(s) comprising (or consisting of) a complementary sequence thereof, polynucleotide(s) hybridizing under stringent conditions to any of these polynucleotides, variant(s) or fragment(s) comprising 15 or more consecutive nucleotides of any of these polynucleotide sequences.

The fragment that may be contained in the kit or the device of the present invention is, for example, one or more, preferably two or more polynucleotides selected from the group consisting of the following polynucleotides (1) to (3):

(1) a polynucleotide comprising 15 or more consecutive nucleotides in a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 by the replacement of u with t, or a complementary sequence thereof;

(2) a polynucleotide comprising 15 or more consecutive nucleotides in a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 by the replacement of u with t, or a complementary sequence thereof; and

(3) a polynucleotide comprising 15 or more consecutive nucleotides in a nucleotide sequence derived from a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 by the replacement of u with t, or a complementary sequence thereof.

In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a polynucleotide consisting of a complementary sequence thereof, a polynucleotide hybridizing under stringent conditions to any of these polynucleotides, or a variant thereof comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a polynucleotide consisting of a complementary sequence thereof, a polynucleotide hybridizing under stringent conditions to any of these polynucleotides, or a variant thereof comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

In a preferred embodiment, the polynucleotide is a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a polynucleotide consisting of a complementary sequence thereof, a polynucleotide hybridizing under stringent conditions to any of these polynucleotides, or a variant thereof comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

In a preferred embodiment, the fragment may be a polynucleotide comprising 15 or more, preferably 17 or more, more preferably 19 or more consecutive nucleotides.

In the present invention, the size of the polynucleotide fragment is the number of nucleotides in the range from, for example, 15 consecutive nucleotides to less than the total number of nucleotides of the sequence, 17 consecutive nucleotides to less than the total number of nucleotides of the sequence, or 19 consecutive nucleotides to less than the total number of nucleotides of the sequence, in the nucleotide sequence of each polynucleotide.

Specific examples of the aforementioned polynucleotide combination constituting the kit or the device of the present invention can include any combination of the polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs shown in Table 1 (SEQ ID NOs: 1 to 224 and 714 to 729 corresponding to the miRNA markers in Table 1) or complementary sequences thereof. However, these are given merely for illustrative purposes, and all of various other possible combinations are included in the present invention.

The aforementioned combination constituting the kit or the device for discriminating a liver cancer patient from a healthy subject according to the present invention is desirably, for example, a combination of two or more of the aforementioned polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs shown in Table 1. Usually, a combination of two of these polynucleotides can produce adequate performance.

The combination of two polynucleotides consisting of the nucleotide sequences or the complementary sequences thereof for specifically discriminating a liver cancer patient from a healthy subject is preferably a combination comprising at least one or more of newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 167 and 714 to 729, among the combinations of two selected from the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 224 and 714 to 729.

The combination of polynucleotides with cancer type specificity capable of discriminating a liver cancer patient not only from a healthy subject but also from other cancer patients is preferably, for example, a combination of a plurality of polynucleotides comprising at least one polynucleotide selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 3, 5, 7, 9, 12, 17, 20, 22, 27, 28, 29, 38, 39, 44, 46, 48, 51, 54, 61, 76, 89, 93, 101, 109, 116, 123, 132, 134, 136, 148, 150, 151, 155, 157, 164, 166, 167, 172, 180, 186, 188, 189, 197, 198, 214, 216, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728 and 729 or complementary sequences thereof (hereinafter, this group is referred to as "cancer type-specific polynucleotide group 1"), with any of the polynucleotides of the other SEQ ID NOs.

The combination of polynucleotides with cancer type specificity capable of discriminating a liver cancer patient not only from a healthy subject but also from other cancer patients is more preferably a combination of a plurality of polynucleotides selected from cancer type-specific polynucleotide group 1.

The combination of polynucleotides with cancer type specificity capable of discriminating a liver cancer patient not only from a healthy subject but also from other cancer patients is more preferably a combination comprising at least one or more polynucleotide(s) selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 3, 7, 9, 22, 38, 44, 134, 148, 155, 157, 164, 167, 172, 214, 714, 715, 716 and 717 or complementary sequences thereof (hereinafter, this group is referred to as "cancer type-specific polynucleotide group 2") included in the cancer type-specific polynucleotide group 1, among the combinations of a plurality of polynucleotides selected from the cancer type-specific polynucleotide group 1.

The number of the polynucleotides with cancer type specificity in the combination described above can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more in the combination and is more preferably 4 or more in the combination. Usually, the combination of 4 of the polynucleotides can produce adequate performance.

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences repre-

sented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are listed below.

(1) a combination of SEQ ID NOs: 1, 7, 9, and 148 (markers: hsa-miR-1343-3p, hsa-miR-6131, hsa-miR-7641, and hsa-miR-642a-3p);

(2) a combination of SEQ ID NOs: 1, 9, 155, and 172 (markers: hsa-miR-1343-3p, hsa-miR-7641, hsa-miR-3131, and hsa-miR-614);

(3) a combination of SEQ ID NOs: 1, 9, 148, and 155 (markers: hsa-miR-1343-3p, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-3131);

(4) a combination of SEQ ID NOs: 1, 155, 172, and 715 (markers: hsa-miR-1343-3p, hsa-miR-3131, hsa-miR-614, and hsa-miR-4448); and

(5) a combination of SEQ ID NOs: 1, 155, 164, and 715 (markers: hsa-miR-1343-3p, hsa-miR-3131, hsa-miR-3162-5p, and hsa-miR-4448).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 3, 7, 9, and 148 (markers: hsa-miR-6515-3p, hsa-miR-6131, hsa-miR-7641, and hsa-miR-642a-3p);

(2) a combination of SEQ ID NOs: 3, 22, 27, and 46 (markers: hsa-miR-6515-3p, hsa-miR-663b, hsa-miR-6729-5p, and hsa-miR-1908-5p);

(3) a combination of SEQ ID NOs: 1, 3, 29, and 155 (markers: hsa-miR-1343-3p, hsa-miR-6515-3p, hsa-miR-4706, and hsa-miR-3131);

(4) a combination of SEQ ID NOs: 1, 3, 151, and 155 (markers: hsa-miR-1343-3p, hsa-miR-6515-3p, hsa-miR-5195-3p, and hsa-miR-3131); and

(5) a combination of SEQ ID NOs: 3, 7, 148, and 715 (markers: hsa-miR-6515-3p, hsa-miR-6131, hsa-miR-642a-3p, and hsa-miR-4448).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 28, 148, and 717 (markers: hsa-miR-6131, hsa-miR-8069, hsa-miR-642a-3p, and hsa-miR-3178);

(2) a combination of SEQ ID NOs: 7, 9, 148, and 186 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-6085);

(3) a combination of SEQ ID NOs: 7, 148, 172, and 715 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-614, and hsa-miR-4448);

(4) a combination of SEQ ID NOs: 7, 9, 148, and 723 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-4745-5p); and

(5) a combination of SEQ ID NOs: 7, 9, 28, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-8069, and hsa-miR-642a-3p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 9 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 157 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-4463);

(2) a combination of SEQ ID NOs: 7, 9, 148, and 722 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-4634);

(3) a combination of SEQ ID NOs: 7, 9, 27, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-6729-5p, and hsa-miR-642a-3p);

(4) a combination of SEQ ID NOs: 7, 9, 148, and 725 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-6803-5p); and

(5) a combination of SEQ ID NOs: 7, 9, 148, and 729 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-6836-3p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 22 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 22, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-663b, and hsa-miR-642a-3p);

(2) a combination of SEQ ID NOs: 7, 22, 28, and 148 (markers: hsa-miR-6131, hsa-miR-663b, hsa-miR-8069, and hsa-miR-642a-3p);

(3) a combination of SEQ ID NOs: 7, 22, 148, and 189 (markers: hsa-miR-6131, hsa-miR-663b, hsa-miR-642a-3p, and hsa-miR-328-5p);

(4) a combination of SEQ ID NOs: 2, 7, 22, and 148 (markers: hsa-miR-6726-5p, hsa-miR-6131, hsa-miR-663b, and hsa-miR-642a-3p); and

(5) a combination of SEQ ID NOs: 7, 22, 148, and 720 (markers: hsa-miR-6131, hsa-miR-663b, hsa-miR-642a-3p, and hsa-miR-6789-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 38 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 38, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-3622a-5p, and hsa-miR-642a-3p);

(2) a combination of SEQ ID NOs: 7, 38, 51, and 148 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-6781-5p, and hsa-miR-642a-3p);

(3) a combination of SEQ ID NOs: 7, 38, 148, and 718 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-4725-3p);

(4) a combination of SEQ ID NOs: 7, 38, 148, and 216 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-1238-5p); and

(5) a combination of SEQ ID NOs: 7, 38, 148, and 728 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-4783-3p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 44 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences

represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 44, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-4665-5p, and hsa-miR-642a-3p);

(2) a combination of SEQ ID NOs: 7, 44, 123, and 148 (markers: hsa-miR-6131, hsa-miR-4665-5p, hsa-miR-4739, and hsa-miR-642a-3p);

(3) a combination of SEQ ID NOs: 7, 38, 44, and 148 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-4665-5p, and hsa-miR-642a-3p);

(4) a combination of SEQ ID NOs: 7, 44, 148, and 723 (markers: hsa-miR-6131, hsa-miR-4665-5p, hsa-miR-642a-3p, and hsa-miR-4745-5p); and

(5) a combination of SEQ ID NOs: 7, 44, 48, and 148 (markers: hsa-miR-6131, hsa-miR-4665-5p, hsa-miR-6765-5p, and hsa-miR-642a-3p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 134 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 134, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-4492, and hsa-miR-642a-3p);

(2) a combination of SEQ ID NOs: 7, 134, 148, and 724 (markers: hsa-miR-6131, hsa-miR-4492, hsa-miR-642a-3p, and hsa-miR-4730);

(3) a combination of SEQ ID NOs: 7, 22, 134, and 148 (markers: hsa-miR-6131, hsa-miR-663b, hsa-miR-4492, and hsa-miR-642a-3p);

(4) a combination of SEQ ID NOs: 7, 134, 148, and 189 (markers: hsa-miR-6131, hsa-miR-4492, hsa-miR-642a-3p, and hsa-miR-328-5p); and

(5) a combination of SEQ ID NOs: 7, 134, 148, and 714 (markers: hsa-miR-6131, hsa-miR-4492, hsa-miR-642a-3p, and hsa-miR-6757-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 148 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 726 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-6798-5p);

(2) a combination of SEQ ID NOs: 7, 9, 148, and 151 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-5195-3p);

(3) a combination of SEQ ID NOs: 7, 9, 109, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-6826-5p, and hsa-miR-642a-3p);

(4) a combination of SEQ ID NOs: 5, 7, 9, and 148 (markers: hsa-miR-4257, hsa-miR-6131, hsa-miR-7641, and hsa-miR-642a-3p); and

(5) a combination of SEQ ID NOs: 7, 9, 76, and 148 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-3917, and hsa-miR-642a-3p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 155 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 155 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-3131);

(2) a combination of SEQ ID NOs: 7, 38, 148, and 155 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-3131);

(3) a combination of SEQ ID NOs: 1, 9, 155, and 167 (markers: hsa-miR-1343-3p, hsa-miR-7641, hsa-miR-3131, and hsa-miR-6724-5p);

(4) a combination of SEQ ID NOs: 1, 3, 155, and 715 (markers: hsa-miR-1343-3p, hsa-miR-6515-3p, hsa-miR-3131, and hsa-miR-4448); and

(5) a combination of SEQ ID NOs: 1, 3, 38, and 155 (markers: hsa-miR-1343-3p, hsa-miR-6515-3p, hsa-miR-3622a-5p, and hsa-miR-3131).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 157 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 48, 157, and 714 (markers: hsa-miR-6131, hsa-miR-6765-5p, hsa-miR-4463, and hsa-miR-6757-5p);

(2) a combination of SEQ ID NOs: 7, 38, 148, and 157 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-4463);

(3) a combination of SEQ ID NOs: 1, 44, 155, and 157 (markers: hsa-miR-1343-3p, hsa-miR-4665-5p, hsa-miR-3131, and hsa-miR-4463);

(4) a combination of SEQ ID NOs: 7, 76, 157, and 714 (markers: hsa-miR-6131, hsa-miR-3917, hsa-miR-4463, and hsa-miR-6757-5p); and

(5) a combination of SEQ ID NOs: 7, 148, 157, and 189 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-4463, and hsa-miR-328-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 164 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 164 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-3162-5p);

(2) a combination of SEQ ID NOs: 7, 76, 164, and 714 (markers: hsa-miR-6131, hsa-miR-3917, hsa-miR-3162-5p, and hsa-miR-6757-5p);

(3) a combination of SEQ ID NOs: 7, 38, 164, and 714 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-3162-5p, and hsa-miR-6757-5p);

(4) a combination of SEQ ID NOs: 7, 38, 148, and 164 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-3162-5p); and

(5) a combination of SEQ ID NOs: 1, 7, 164, and 714 (markers: hsa-miR-1343-3p, hsa-miR-6131, hsa-miR-3162-5p, and hsa-miR-6757-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 167 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 167 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-6724-5p);

(2) a combination of SEQ ID NOs: 1, 7, 167, and 714 (markers: hsa-miR-1343-3p, hsa-miR-6131, hsa-miR-6724-5p, and hsa-miR-6757-5p);

(3) a combination of SEQ ID NOs: 7, 151, 167, and 714 (markers: hsa-miR-6131, hsa-miR-5195-3p, hsa-miR-6724-5p, and hsa-miR-6757-5p);

(4) a combination of SEQ ID NOs: 7, 148, 167, and 189 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-6724-5p, and hsa-miR-328-5p); and

(5) a combination of SEQ ID NOs: 7, 28, 167, and 714 (markers: hsa-miR-6131, hsa-miR-8069, hsa-miR-6724-5p, and hsa-miR-6757-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 172 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 172 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-614);

(2) a combination of SEQ ID NOs: 7, 150, 172, and 714 (markers: hsa-miR-6131, hsa-miR-4728-5p, hsa-miR-614, and hsa-miR-6757-5p);

(3) a combination of SEQ ID NOs: 7, 172, 714, and 715 (markers: hsa-miR-6131, hsa-miR-614, hsa-miR-6757-5p, and hsa-miR-4448);

(4) a combination of SEQ ID NOs: 7, 38, 155, and 172 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-3131, and hsa-miR-614); and

(5) a combination of SEQ ID NOs: 1, 2, 155, and 172 (markers: hsa-miR-1343-3p, hsa-miR-6726-5p, hsa-miR-3131, and hsa-miR-614).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 214 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 214 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-4723-5p);

(2) a combination of SEQ ID NOs: 7, 148, 189, and 214 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-328-5p, and hsa-miR-4723-5p);

(3) a combination of SEQ ID NOs: 2, 7, 148, and 214 (markers: hsa-miR-6726-5p, hsa-miR-6131, hsa-miR-642a-3p, and hsa-miR-4723-5p);

(4) a combination of SEQ ID NOs: 1, 7, 214, and 714 (markers: hsa-miR-1343-3p, hsa-miR-6131, hsa-miR-4723-5p, and hsa-miR-6757-5p); and

(5) a combination of SEQ ID NOs: 7, 39, 148, and 214 (markers: hsa-miR-6131, hsa-miR-615-5p, hsa-miR-642a-3p, and hsa-miR-4723-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 714 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 714 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-6757-5p);

(2) a combination of SEQ ID NOs: 7, 54, 148, and 714 (markers: hsa-miR-6131, hsa-miR-6784-5p, hsa-miR-642a-3p, and hsa-miR-6757-5p);

(3) a combination of SEQ ID NOs: 7, 148, 151, and 714 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-5195-3p, and hsa-miR-6757-5p);

(4) a combination of SEQ ID NOs: 7, 38, 148, and 714 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-6757-5p); and

(5) a combination of SEQ ID NOs: 7, 28, 148, and 714 (markers: hsa-miR-6131, hsa-miR-8069, hsa-miR-642a-3p, and hsa-miR-6757-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 715 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 2, 7, 148, and 715 (markers: hsa-miR-6726-5p, hsa-miR-6131, hsa-miR-642a-3p, and hsa-miR-4448);

(2) a combination of SEQ ID NOs: 7, 9, 148, and 715 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-4448);

(3) a combination of SEQ ID NOs: 7, 17, 148, and 715 (markers: hsa-miR-6131, hsa-miR-204-3p, hsa-miR-642a-3p, and hsa-miR-4448);

(4) a combination of SEQ ID NOs: 7, 38, 148, and 715 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-4448); and

(5) a combination of SEQ ID NOs: 7, 148, 715, and 725 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-6803-5p, and hsa-miR-4448).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 716 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 716 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-671-5p);

(2) a combination of SEQ ID NOs: 7, 148, 714, and 716 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-6757-5p, and hsa-miR-671-5p);

(3) a combination of SEQ ID NOs: 2, 7, 148, and 716 (markers: hsa-miR-6726-5p, hsa-miR-6131, hsa-miR-642a-3p, and hsa-miR-671-5p);

(4) a combination of SEQ ID NOs: 7, 38, 148, and 716 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-671-5p); and

(5) a combination of SEQ ID NOs: 7, 148, 715, and 716 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-4448, and hsa-miR-671-5p).

Non-limiting examples of the combination of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 717 or a complementary sequence thereof with polynucleotides consisting of nucleotide sequences represented by SEQ ID NOs of three polynucleotides selected from the cancer type-specific polynucleotide group 1 or complementary sequences thereof are further listed below.

(1) a combination of SEQ ID NOs: 7, 9, 148, and 717 (markers: hsa-miR-6131, hsa-miR-7641, hsa-miR-642a-3p, and hsa-miR-3178);

(2) a combination of SEQ ID NOs: 7, 38, 148, and 717 (markers: hsa-miR-6131, hsa-miR-3622a-5p, hsa-miR-642a-3p, and hsa-miR-3178);

(3) a combination of SEQ ID NOs: 7, 27, 148, and 717 (markers: hsa-miR-6131, hsa-miR-6729-5p, hsa-miR-642a-3p, and hsa-miR-3178);

(4) a combination of SEQ ID NOs: 7, 44, 148, and 717 (markers: hsa-miR-6131, hsa-miR-4665-5p, hsa-miR-642a-3p, and hsa-miR-3178); and

(5) a combination of SEQ ID NOs: 7, 148, 715, and 717 (markers: hsa-miR-6131, hsa-miR-642a-3p, hsa-miR-4448, and hsa-miR-3178).

The kit or the device of the present invention may also comprise a polynucleotide that is already known or that will be found in the future, to enable detection of liver cancer, in addition to the polynucleotide(s) (which can include variant(s), fragment(s), and derivative(s)) according to the present invention described above.

The kit of the present invention may also comprise an antibody for measuring a marker for liver cancer examination known in the art, such as AFP, CEA, CA19-9 and PIVKA-II, in addition to the polynucleotide(s) according to the present invention as described above.

These polynucleotides contained in the kit of the present invention may be packaged in different containers either individually or in any combination.

The kit of the present invention may comprise a kit for extracting a nucleic acid (e.g., total RNA) from body fluids, cells, or tissues, a fluorescent material for labeling, an enzyme and a medium for nucleic acid amplification, an instruction manual, etc.

The device of the present invention is a device for cancer marker measurement in which nucleic acids such as the polynucleotides according to the present invention described above are bonded or attached to, for example, a solid phase. Examples of the material for the solid phase include plastics, paper, glass, and silicon. The material for the solid phase is preferably a plastic from the viewpoint of easy processability. The solid phase has any shape and is, for example, square, round, reed-shaped, or film-shaped. The device of the present invention includes, for example, a device for measurement by a hybridization technique. Specific examples thereof include blotting devices and nucleic acid arrays (e.g., microarrays, DNA chips, and RNA chips).

The nucleic acid array technique is a technique which involves bonding or attaching the nucleic acids one by one by use of a method [e.g., a method of spotting the nucleic acids using a high-density dispenser called spotter or arrayer onto the surface of the solid phase surface-treated, if necessary, by coating with L-lysine or the introduction of a functional group such as an amino group or a carboxyl group, a method of spraying the nucleic acids onto the solid phase using an inkjet which injects very small liquid droplets by a piezoelectric element or the like from a nozzle, or a method of sequentially synthesizing nucleotides on the solid phase] to prepare an array such as a chip and measuring a target nucleic acid through the use of hybridization using this array.

The kit or the device of the present invention comprises nucleic acids capable of specifically binding to the polynucleotides of at least one or more, preferably at least two or more, more preferably at least three or more, most preferably at least five or more to all of the liver cancer marker miRNAs, respectively, of the group 1 described above. The kit or the device of the present invention may optionally further comprise nucleic acids capable of specifically binding to the polynucleotides of at least one or more, preferably at least two or more, more preferably at least three or more, most preferably at least five or more to all of the liver cancer marker miRNAs, respectively, of the group 2 described above. The kit or the device of the present invention may optionally further comprise nucleic acids capable of specifically binding to the polynucleotides of at least one or more, preferably at least two or more, more preferably at least three or more, most preferably at least five or more to all of the liver cancer marker miRNAs, respectively, of the group 3 described above.

The kit or the device of the present invention can be used for detecting liver cancer as described in Section 4 below.

4. Method for Detecting Liver Cancer

The present invention further provides a method for detecting liver cancer, comprising using the kit or the device of the present invention (comprising the above-mentioned nucleic acid(s) that can be used in the present invention) described in Section 3 above to measure expression level(s) of one or more liver cancer-derived gene(s) being an expression level of liver cancer-derived gene(s) selected from the following group: miR-1343-3p, miR-6726-5p, miR-6515-3p, miR-4651, miR-4257, miR-3188, miR-6131, miR-6766-3p, miR-7641, miR-1249, miR-3679-3p, miR-6787-5p, miR-4454, miR-3135b, miR-6765-3p, miR-7975, miR-204-3p, miR-7977, miR-7110-5p, miR-6717-5p, miR-6870-5p, miR-663b, miR-6875-5p, miR-8072, miR-6816-5p, miR-4281, miR-6729-5p, miR-8069, miR-4706, miR-7108-5p, miR-4433b-3p, miR-6893-5p, miR-6857-5p, miR-1227-5p, miR-6741-5p, miR-451a, miR-8063, miR-3622a-5p, miR-615-5p, miR-128-1-5p, miR-6825-5p, miR-1260b, miR-4433-3p, miR-4665-5p, miR-7845-5p, miR-1908-5p, miR-6840-3p, miR-6765-5p, miR-296-5p, miR-3675-3p, miR-6781-5p, miR-423-5p, miR-3663-3p, miR-6784-5p, miR-6749-5p, miR-1231, miR-4746-3p, miR-6780b-5p, miR-4758-5p, miR-3679-5p, miR-3184-5p, miR-6125, miR-6721-5p, miR-6791-5p, miR-3185, miR-1260a, miR-3197, miR-6845-5p, miR-6887-5p, miR-6738-5p, miR-6872-3p, miR-4497, miR-1229-5p, miR-6820-5p, miR-6777-5p, miR-3917, miR-5787, miR-4286, miR-6877-5p, miR-1225-3p, miR-6088, miR-6800-5p, miR-1246, miR-4467, miR-4419b, miR-1914-3p, miR-4632-5p, miR-1915-5p, miR-3940-5p, miR-1185-2-3p, miR-6746-5p, miR-5001-5p, miR-1228-5p, miR-5572, miR-4327, miR-4638-5p, miR-6799-5p, miR-6861-5p, miR-6727-5p, miR-4513, miR-6805-3p, miR-6808-5p, miR-4449, miR-1199-5p, miR-1275, miR-4792, miR-4443, miR-6891-5p, miR-6826-5p, miR-6807-5p, miR-7150, miR-4534, miR-4476, miR-4649-5p, miR-4525, miR-1915-3p, miR-4516, miR-4417, miR-642b-3p, miR-3141, miR-5100, miR-6848-5p, miR-4739, miR-4459, miR-1237-5p, miR-296-3p, miR-4665-3p, miR-

6786-5p, miR-4258, miR-6510-5p, miR-1343-5p, miR-1247-3p, miR-6805-5p, miR-4492, miR-1469, miR-1268b, miR-6858-5p, miR-3937, miR-939-5p, miR-3656, miR-744-5p, miR-4687-3p, miR-4763-3p, miR-3620-5p, miR-3195, miR-6842-5p, miR-4707-5p, miR-642a-3p, miR-7113-3p, miR-4728-5p, miR-5195-3p, miR-1185-1-3p, miR-6774-5p, miR-8059, miR-3131, miR-7847-3p, miR-4463, miR-128-2-5p, miR-4508, miR-6806-5p, miR-7111-5p, miR-6782-5p, miR-4734, miR-3162-5p, miR-887-3p, miR-6752-5p, miR-6724-5p, miR-6757-5p, miR-4448, miR-671-5p, miR-3178, miR-4725-3p, miR-940, miR-6789-5p, miR-4484, miR-4634, miR-4745-5p, miR-4730, miR-6803-5p, miR-6798-5p, miR-3648, miR-4783-3p and miR-6836-3p; optionally an expression level of liver cancer-derived gene(s) selected from the following group: miR-23b-3p, miR-23a-3p, miR-625-3p, miR-1228-3p, miR-614, miR-1913, miR-92a-2-5p, miR-187-5p, miR-16-5p, miR-92b-3p, miR-150-3p, miR-564, miR-125a-3p, miR-92b-5p, miR-92a-3p and miR-663a; and optionally an expression level of liver cancer-derived gene(s) selected from miR-4688, miR-4648, miR-6085, miR-6126, miR-6880-5p, miR-328-5p, miR-6768-5p, miR-3180, miR-6087, miR-1273g-3p, miR-1225-5p, miR-3196, miR-4695-5p, miR-6732-5p, miR-638, miR-6813-5p, miR-665, miR-486-3p, miR-4466, miR-30c-1-3p, miR-3621, miR-6743-5p, miR-4298, miR-4741, miR-3619-3p, miR-6824-5p, miR-5698, miR-371a-5p, miR-4488, miR-1233-5p, miR-4723-5p, miR-24-3p, miR-1238-5p, miR-4442, miR-3928-3p, miR-6716-5p, miR-6089, miR-6124, miR-6778-5p, miR-557 and miR-6090 in a sample in vitro, further comparing, for example, the expression level(s) of the aforementioned gene(s) in the sample (e.g., blood, serum, or plasma) collected from a subject suspected of having liver cancer with a control expression level in the sample collected from a healthy subject (including a non-liver cancer patient), and evaluating the subject as having liver cancer when the expression level(s) of the target nucleic acid(s) is statistically significantly different between the samples.

This method of the present invention enables a limitedly invasive, early diagnosis of the cancer with high sensitivity and high specificity and thereby brings about early treatment and improved prognosis. In addition, exacerbation of the disease or the effectiveness of surgical, radiotherapeutic, and chemotherapeutic treatments can be monitored.

The method for extracting the liver cancer-derived gene from the sample such as blood, serum, or plasma according to the present invention is particularly preferably prepared by the addition of a reagent for RNA extraction in 3D-Gene® RNA extraction reagent from liquid sample kit (Toray Industries, Inc.). A general acidic phenol method (acid guanidinium-phenol-chloroform (AGPC)) may be used, or Trizol® (Life Technologies Corp.) may be used. The liver cancer-derived gene may be prepared by the addition of a reagent for RNA extraction containing acidic phenol, such as Trizol (Life Technologies Corp.) or Isogen (Nippon Gene Co., Ltd.). Alternatively, a kit such as miRNeasy® Mini Kit (Qiagen N.V.) can be used, though the method is not limited thereto.

The present invention also provides use of the kit or the device of the present invention for detecting in vitro an expression product of a liver cancer-derived miRNA gene in a sample derived from a subject.

In the method of the present invention, the kit or device described above comprising a single polynucleotide or any possible combination of the polynucleotides that can be used in the present invention as described above is used.

In the detection or (genetic) diagnosis of liver cancer according to the present invention, each polynucleotide contained in the kit or the device of the present invention can be used as a probe or a primer. In the case of using the polynucleotide as a primer, TaqMan® MicroRNA Assays from Life Technologies Corp., miScript PCR System from Qiagen N.V., or the like can be used, though the method is not limited thereto.

The polynucleotide contained in the kit or the device of the present invention can be used as a primer or a probe according to a routine method in a method known in the art for specifically detecting the particular gene, for example, a hybridization technique such as Northern blot, Southern blot, in situ hybridization, Northern hybridization, or Southern hybridization, or a quantitative amplification technique such as quantitative RT-PCR. A body fluid such as blood, serum, plasma, or urine of the subject is collected as a sample to be assayed according to the type of the detection method used. Alternatively, total RNA prepared from such a body fluid by the method described above may be used, and various polynucleotides including cDNA prepared on the basis of the RNA may be used.

The kit or the device of the present invention is useful for the diagnosis of liver cancer or the detection of the presence or absence of liver cancer. Specifically, the detection of liver cancer using the kit or the device can be performed by detecting in vitro an expression level of a gene using the nucleic acid probe or the primer contained in the kit or the device in a sample such as blood, serum, plasma, or urine from a subject suspected of having liver cancer. The subject suspected of having liver cancer can be evaluated as having liver cancer when the expression level of a target miRNA marker measured using polynucleotide(s) (including variant(s), fragment(s), and derivative(s) thereof) consisting of a nucleotide sequence represented by at least one or more of SEQ ID NOs: 1 to 167 and 714 to 729 or a complementary sequence thereof, optionally a nucleotide sequence represented by one or more of SEQ ID NOs: 168 to 183 or a complementary sequence thereof, and optionally a nucleotide sequence represented by one or more of SEQ ID NOs: 184 to 224 or a complementary sequence thereof in the sample such as blood, serum, plasma, or urine of the subject is statistically significantly different compared with the expression level thereof in the sample such as blood, serum, or plasma, or urine of a healthy subject.

The method of the present invention can be combined with a diagnostic imaging method such as ultrasonography, CT scanning, MRI scanning, or angiography examination. The method of the present invention is capable of specifically detecting liver cancer and can substantially discriminate liver cancer from the other cancers.

The method for detecting the absence of an expression product of a liver cancer-derived gene or the presence of the expression product of a liver cancer-derived gene in a sample using the kit or the device of the present invention comprises collecting a body fluid such as blood, serum, plasma, or urine of a subject, and measuring the expression level of the target gene contained therein using one or more polynucleotide(s) (including variant(s), fragment(s), or derivative(s)) selected from the polynucleotide group of the present invention, to evaluate the presence or absence of liver cancer or to detect liver cancer. Using the method for detecting liver cancer according to the present invention, for example, the presence or absence of amelioration of the disease or the degree of amelioration thereof in a liver cancer

patient when a therapeutic drug is administered to the patient for amelioration of the disease can be also evaluated or diagnosed.

The method of the present invention may comprise, for example, the following steps (a), (b), and (c):

(a) a step of contacting in vitro a sample derived from a subject with a polynucleotide in the kit or the device of the present invention;

(b) a step of measuring an expression level of the target nucleic acid in the sample using the polynucleotide as a nucleic acid probe or a primer; and

(c) a step of evaluating the presence or absence of liver cancer (cells) in the subject on the basis of a measurement result obtained in the step (b).

Specifically, the present invention provides a method for detecting liver cancer, comprising measuring an expression level of a target nucleic acid in a sample of a subject using nucleic acid(s) capable of specifically binding to at least one or more (preferably at least two or more) polynucleotide(s) selected from the group consisting of miR-1343-3p, miR-6726-5p, miR-6515-3p, miR-4651, miR-4257, miR-3188, miR-6131, miR-6766-3p, miR-7641, miR-1249, miR-3679-3p, miR-6787-5p, miR-4454, miR-3135b, miR-6765-3p, miR-7975, miR-204-3p, miR-7977, miR-7110-5p, miR-6717-5p, miR-6870-5p, miR-663b, miR-6875-5p, miR-8072, miR-6816-5p, miR-4281, miR-6729-5p, miR-8069, miR-4706, miR-7108-5p, miR-4433b-3p, miR-6893-5p, miR-6857-5p, miR-1227-5p, miR-6741-5p, miR-451a, miR-8063, miR-3622a-5p, miR-615-5p, miR-128-1-5p, miR-6825-5p, miR-1260b, miR-4433-3p, miR-4665-5p, miR-7845-5p, miR-1908-5p, miR-6840-3p, miR-6765-5p, miR-296-5p, miR-3675-3p, miR-6781-5p, miR-423-5p, miR-3663-3p, miR-6784-5p, miR-6749-5p, miR-1231, miR-4746-3p, miR-6780b-5p, miR-4758-5p, miR-3679-5p, miR-3184-5p, miR-6125, miR-6721-5p, miR-6791-5p, miR-3185, miR-1260a, miR-3197, miR-6845-5p, miR-6887-5p, miR-6738-5p, miR-6872-3p, miR-4497, miR-1229-5p, miR-6820-5p, miR-6777-5p, miR-3917, miR-5787, miR-4286, miR-6877-5p, miR-1225-3p, miR-6088, miR-6800-5p, miR-1246, miR-4467, miR-4419b, miR-1914-3p, miR-4632-5p, miR-1915-5p, miR-3940-5p, miR-1185-2-3p, miR-6746-5p, miR-5001-5p, miR-1228-5p, miR-5572, miR-4327, miR-4638-5p, miR-6799-5p, miR-6861-5p, miR-6727-5p, miR-4513, miR-6805-3p, miR-6808-5p, miR-4449, miR-1199-5p, miR-1275, miR-4792, miR-4443, miR-6891-5p, miR-6826-5p, miR-6807-5p, miR-7150, miR-4534, miR-4476, miR-4649-5p, miR-4525, miR-1915-3p, miR-4516, miR-4417, miR-642b-3p, miR-3141, miR-5100, miR-6848-5p, miR-4739, miR-4459, miR-1237-5p, miR-296-3p, miR-4665-3p, miR-6786-5p, miR-4258, miR-6510-5p, miR-1343-5p, miR-1247-3p, miR-6805-5p, miR-4492, miR-1469, miR-1268b, miR-6858-5p, miR-3937, miR-939-5p, miR-3656, miR-744-5p, miR-4687-3p, miR-4763-3p, miR-3620-5p, miR-3195, miR-6842-5p, miR-4707-5p, miR-642a-3p, miR-7113-3p, miR-4728-5p, miR-5195-3p, miR-1185-1-3p, miR-6774-5p, miR-8059, miR-3131, miR-7847-3p, miR-4463, miR-128-2-5p, miR-4508, miR-6806-5p, miR-7111-5p, miR-6782-5p, miR-4734, miR-3162-5p, miR-887-3p, miR-6752-5p, miR-6724-5p, miR-6757-5p, miR-4448, miR-671-5p, miR-3178, miR-4725-3p, miR-940, miR-6789-5p, miR-4484, miR-4634, miR-4745-5p, miR-4730, miR-6803-5p, miR-6798-5p, miR-3648, miR-4783-3p and miR-6836-3p, and evaluating in vitro whether or not the subject has liver cancer using the measured expression level and a control expression level of a healthy subject measured in the same way as above.

The term "evaluation" used herein is evaluation support based on results of in vitro examination, not physician's judgment.

As described above, in a preferred embodiment of the method of the present invention, specifically, miR-1343-3p is hsa-miR-1343-3p, miR-6726-5p is hsa-miR-6726-5p, miR-6515-3p is hsa-miR-6515-3p, miR-4651 is hsa-miR-4651, miR-4257 is hsa-miR-4257, miR-3188 is hsa-miR-3188, miR-6131 is hsa-miR-6131, miR-6766-3p is hsa-miR-6766-3p, miR-7641 is hsa-miR-7641, miR-1249 is hsa-miR-1249, miR-3679-3p is hsa-miR-3679-3p, miR-6787-5p is hsa-miR-6787-5p, miR-4454 is hsa-miR-4454, miR-3135b is hsa-miR-3135b, miR-6765-3p is hsa-miR-6765-3p, miR-7975 is hsa-miR-7975, miR-204-3p is hsa-miR-204-3p, miR-7977 is hsa-miR-7977, miR-7110-5p is hsa-miR-7110-5p, miR-6717-5p is hsa-miR-6717-5p, miR-6870-5p is hsa-miR-6870-5p, miR-663b is hsa-miR-663b, miR-6875-5p is hsa-miR-6875-5p, miR-8072 is hsa-miR-8072, miR-6816-5p is hsa-miR-6816-5p, miR-4281 is hsa-miR-4281, miR-6729-5p is hsa-miR-6729-5p, miR-8069 is hsa-miR-8069, miR-4706 is hsa-miR-4706, miR-7108-5p is hsa-miR-7108-5p, miR-4433b-3p is hsa-miR-4433b-3p, miR-6893-5p is hsa-miR-6893-5p, miR-6857-5p is hsa-miR-6857-5p, miR-1227-5p is hsa-miR-1227-5p, miR-6741-5p is hsa-miR-6741-5p, miR-451a is hsa-miR-451a, miR-8063 is hsa-miR-8063, miR-3622a-5p is hsa-miR-3622a-5p, miR-615-5p is hsa-miR-615-5p, miR-128-1-5p is hsa-miR-128-1-5p, miR-6825-5p is hsa-miR-6825-5p, miR-1260b is hsa-miR-1260b, miR-4433-3p is hsa-miR-4433-3p, miR-4665-5p is hsa-miR-4665-5p, miR-7845-5p is hsa-miR-7845-5p, miR-1908-5p is hsa-miR-1908-5p, miR-6840-3p is hsa-miR-6840-3p, miR-6765-5p is hsa-miR-6765-5p, miR-296-5p is hsa-miR-296-5p, miR-3675-3p is hsa-miR-3675-3p, miR-6781-5p is hsa-miR-6781-5p, miR-423-5p is hsa-miR-423-5p, miR-3663-3p is hsa-miR-3663-3p, miR-6784-5p is hsa-miR-6784-5p, miR-6749-5p is hsa-miR-6749-5p, miR-1231 is hsa-miR-1231, miR-4746-3p is hsa-miR-4746-3p, miR-6780b-5p is hsa-miR-6780b-5p, miR-4758-5p is hsa-miR-4758-5p, miR-3679-5p is hsa-miR-3679-5p, miR-3184-5p is hsa-miR-3184-5p, miR-6125 is hsa-miR-6125, miR-6721-5p is hsa-miR-6721-5p, miR-6791-5p is hsa-miR-6791-5p, miR-3185 is hsa-miR-3185, miR-1260a is hsa-miR-1260a, miR-3197 is hsa-miR-3197, miR-6845-5p is hsa-miR-6845-5p, miR-6887-5p is hsa-miR-6887-5p, miR-6738-5p is hsa-miR-6738-5p, miR-6872-3p is hsa-miR-6872-3p, miR-4497 is hsa-miR-4497, miR-1229-5p is hsa-miR-1229-5p, miR-6820-5p is hsa-miR-6820-5p, miR-6777-5p is hsa-miR-6777-5p, miR-3917 is hsa-miR-3917, miR-5787 is hsa-miR-5787, miR-4286 is hsa-miR-4286, miR-6877-5p is hsa-miR-6877-5p, miR-1225-3p is hsa-miR-1225-3p, miR-6088 is hsa-miR-6088, miR-6800-5p is hsa-miR-6800-5p, miR-1246 is hsa-miR-1246, miR-4467 is hsa-miR-4467, miR-4419b is hsa-miR-4419b, miR-1914-3p is hsa-miR-1914-3p, miR-4632-5p is hsa-miR-4632-5p, miR-1915-5p is hsa-miR-1915-5p, miR-3940-5p is hsa-miR-3940-5p, miR-1185-2-3p is hsa-miR-1185-2-3p, miR-6746-5p is hsa-miR-6746-5p, miR-5001-5p is hsa-miR-5001-5p, miR-1228-5p is hsa-miR-1228-5p, miR-5572 is hsa-miR-5572, miR-4327 is hsa-miR-4327, miR-4638-5p is hsa-miR-4638-5p, miR-6799-5p is hsa-miR-6799-5p, miR-6861-5p is hsa-miR-6861-5p, miR-6727-5p is hsa-miR-6727-5p, miR-4513 is hsa-miR-4513, miR-6805-3p is hsa-miR-6805-3p, miR-6808-5p is hsa-miR-6808-5p, miR-4449 is hsa-miR-4449, miR-1199-5p is hsa-miR-1199-5p, miR-1275 is hsa-miR-1275, miR-4792 is hsa-miR-4792, miR-4443 is hsa-miR-4443, miR-6891-5p is hsa-miR-6891-5p, miR-6826-5p is hsa-miR-6826-5p, miR-6807-5p is hsa-miR-6807-5p, miR-

7150 is hsa-miR-7150, miR-4534 is hsa-miR-4534, miR-4476 is hsa-miR-4476, miR-4649-5p is hsa-miR-4649-5p, miR-4525 is hsa-miR-4525, miR-1915-3p is hsa-miR-1915-3p, miR-4516 is hsa-miR-4516, miR-4417 is hsa-miR-4417, miR-642b-3p is hsa-miR-642b-3p, miR-3141 is hsa-miR-3141, miR-5100 is hsa-miR-5100, miR-6848-5p is hsa-miR-6848-5p, miR-4739 is hsa-miR-4739, miR-4459 is hsa-miR-4459, miR-1237-5p is hsa-miR-1237-5p, miR-296-3p is hsa-miR-296-3p, miR-4665-3p is hsa-miR-4665-3p, miR-6786-5p is hsa-miR-6786-5p, miR-4258 is hsa-miR-4258, miR-6510-5p is hsa-miR-6510-5p, miR-1343-5p is hsa-miR-1343-5p, miR-1247-3p is hsa-miR-1247-3p, miR-6805-5p is hsa-miR-6805-5p, miR-4492 is hsa-miR-4492, miR-1469 is hsa-miR-1469, miR-1268b is hsa-miR-1268b, miR-6858-5p is hsa-miR-6858-5p, miR-3937 is hsa-miR-3937, miR-939-5p is hsa-miR-939-5p, miR-3656 is hsa-miR-3656, miR-744-5p is hsa-miR-744-5p, miR-4687-3p is hsa-miR-4687-3p, miR-4763-3p is hsa-miR-4763-3p, miR-3620-5p is hsa-miR-3620-5p, miR-3195 is hsa-miR-3195, miR-6842-5p is hsa-miR-6842-5p, miR-4707-5p is hsa-miR-4707-5p, miR-642a-3p is hsa-miR-642a-3p, miR-7113-3p is hsa-miR-7113-3p, miR-4728-5p is hsa-miR-4728-5p, miR-5195-3p is hsa-miR-5195-3p, miR-1185-1-3p is hsa-miR-1185-1-3p, miR-6774-5p is hsa-miR-6774-5p, miR-8059 is hsa-miR-8059, miR-3131 is hsa-miR-3131, miR-7847-3p is hsa-miR-7847-3p, miR-4463 is hsa-miR-4463, miR-128-2-5p is hsa-miR-128-2-5p, miR-4508 is hsa-miR-4508, miR-6806-5p is hsa-miR-6806-5p, miR-7111-5p is hsa-miR-7111-5p, miR-6782-5p is hsa-miR-6782-5p, miR-4734 is hsa-miR-4734, miR-3162-5p is hsa-miR-3162-5p, miR-887-3p is hsa-miR-887-3p, miR-6752-5p is hsa-miR-6752-5p, miR-6724-5p is hsa-miR-6724-5p, miR-6757-5p is hsa-miR-6757-5p, miR-4448 is hsa-miR-4448, miR-671-5p is hsa-miR-671-5p, miR-3178 is hsa-miR-3178, miR-4725-3p is hsa-miR-4725-3p, miR-940 is hsa-miR-940, miR-6789-5p is hsa-miR-6789-5p, miR-4484 is hsa-miR-4484, miR-4634 is hsa-miR-4634, miR-4745-5p is hsa-miR-4745-5p, miR-4730 is hsa-miR-4730, miR-6803-5p is hsa-miR-6803-5p, miR-6798-5p is hsa-miR-6798-5p, miR-3648 is hsa-miR-3648, miR-4783-3p is hsa-miR-4783-3p, and miR-6836-3p is hsa-miR-6836-3p.

In a preferred embodiment of the method of the present invention, specifically, the nucleic acid (specifically, probe or primer) is selected from the group consisting of the following polynucleotides (a) to (e):

(a) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(b) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729,

(c) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(d) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(e) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (a) to (d).

In the method of the present invention, nucleic acid(s) capable of specifically binding to at least one or more polynucleotide(s) selected from the followings: miR-23b-3p, miR-23a-3p, miR-625-3p, miR-1228-3p, miR-614, miR-1913, miR-92a-2-5p, miR-187-5p, miR-16-5p, miR-92b-3p, miR-150-3p, miR-564, miR-125a-3p, miR-92b-5p, miR-92a-3p and miR-663a may be further used.

In a preferred embodiment, as for such an additional nucleic acid, specifically, miR-23b-3p is hsa-miR-23b-3p, miR-23a-3p is hsa-miR-23a-3p, miR-625-3p is hsa-miR-625-3p, miR-1228-3p is hsa-miR-1228-3p, miR-614 is hsa-miR-614, miR-1913 is hsa-miR-1913, miR-92a-2-5p is hsa-miR-92a-2-5p, miR-187-5p is hsa-miR-187-5p, miR-16-5p is hsa-miR-16-5p, miR-92b-3p is hsa-miR-92b-3p, miR-150-3p is hsa-miR-150-3p, miR-564 is hsa-miR-564, miR-125a-3p is hsa-miR-125a-3p, miR-92b-5p is hsa-miR-92b-5p, miR-92a-3p is hsa-miR-92a-3p, and miR-663a is hsa-miR-663a.

In a preferred embodiment, such a nucleic acid is specifically selected from the group consisting of the following polynucleotides (f) to (j):

(f) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(g) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183,

(h) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides, (i) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(j) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (f) to (i).

In the method of the present invention, a nucleic acid capable of specifically binding to at least one or more polynucleotide(s) selected from the group consisting of miR-4688, miR-4648, miR-6085, miR-6126, miR-6880-5p, miR-328-5p, miR-6768-5p, miR-3180, miR-6087, miR-1273g-3p, miR-1225-5p, miR-3196, miR-4695-5p, miR-6732-5p, miR-638, miR-6813-5p, miR-665, miR-486-3p, miR-4466, miR-30c-1-3p, miR-3621, miR-6743-5p, miR-4298, miR-4741, miR-3619-3p, miR-6824-5p, miR-5698, miR-371a-5p, miR-4488, miR-1233-5p, miR-4723-5p, miR-24-3p, miR-1238-5p, miR-4442, miR-3928-3p, miR-6716-5p, miR-6089, miR-6124, miR-6778-5p, miR-557 and miR-6090 may be further used.

In a preferred embodiment, as for such an additional nucleic acid, specifically, miR-4688 is hsa-miR-4688, miR-4648 is hsa-miR-4648, miR-6085 is hsa-miR-6085, miR-6126 is hsa-miR-6126, miR-6880-5p is hsa-miR-6880-5p, miR-328-5p is hsa-miR-328-5p, miR-6768-5p is hsa-miR-6768-5p, miR-3180 is hsa-miR-3180, miR-6087 is hsa-miR-6087, miR-1273g-3p is hsa-miR-1273g-3p, miR-1225-5p is hsa-miR-1225-5p, miR-3196 is hsa-miR-3196, miR-4695-5p is hsa-miR-4695-5p, miR-6732-5p is hsa-miR-6732-5p, miR-638 is hsa-miR-638, miR-6813-5p is hsa-miR-6813-5p, miR-665 is hsa-miR-665, miR-486-3p is hsa-miR-486-3p, miR-4466 is hsa-miR-4466, miR-30c-1-3p is hsa-miR-30c-1-3p, miR-3621 is hsa-miR-3621, miR-6743-5p is hsa-

miR-6743-5p, miR-4298 is hsa-miR-4298, miR-4741 is hsa-miR-4741, miR-3619-3p is hsa-miR-3619-3p, miR-6824-5p is hsa-miR-6824-5p, miR-5698 is hsa-miR-5698, miR-371a-5p is hsa-miR-371a-5p, miR-4488 is hsa-miR-4488, miR-1233-5p is hsa-miR-1233-5p, miR-4723-5p is hsa-miR-4723-5p, miR-24-3p is hsa-miR-24-3p, miR-1238-5p is hsa-miR-1238-5p, miR-4442 is hsa-miR-4442, miR-3928-3p is hsa-miR-3928-3p, miR-6716-5p is hsa-miR-6716-5p, miR-6089 is hsa-miR-6089, miR-6124 is hsa-miR-6124, miR-6778-5p is hsa-miR-6778-5p, miR-557 is hsa-miR-557, and miR-6090 is hsa-miR-6090.

In a preferred embodiment, such a nucleic acid is specifically a polynucleotide selected from the group consisting of the following polynucleotides (k) to (o):

(k) a polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(l) a polynucleotide comprising a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224,

(m) a polynucleotide consisting of a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, a variant thereof, a derivative thereof, or a fragment thereof comprising 15 or more consecutive nucleotides,

(n) a polynucleotide comprising a nucleotide sequence complementary to a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a nucleotide sequence derived from the nucleotide sequence by the replacement of u with t, and

(o) a polynucleotide hybridizing under stringent conditions to any of the polynucleotides (k) to (n).

Examples of the sample used in the method of the present invention can include samples prepared from a living tissue (preferably a liver tissue) or a body fluid such as blood, serum, plasma, or urine of the subject. Specifically, for example, an RNA-containing sample prepared from the tissue, a polynucleotide-containing sample further prepared therefrom, a body fluid such as blood, serum, plasma, or urine, a portion or the whole of a living tissue collected from the subject by biopsy or the like, or a living tissue excised by surgery can be used, and the sample for measurement can be prepared therefrom.

The subject used herein refers to a mammal, for example, a human, a monkey, a mouse and a rat without any limitation, and is preferably a human.

The steps of the method of the present invention can be changed according to the type of the sample to be assayed.

In the case of using RNA as an analyte, the detection of liver cancer (cells) may comprise, for example, the following steps (a), (b), and (c):

(a) a step of binding RNA prepared from the sample of a subject or a complementary polynucleotide (cDNA) transcribed therefrom to a polynucleotide in the kit or the device of the present invention;

(b) a step of measuring the sample-derived RNA or the cDNA synthesized from the RNA, bound with the polynucleotide by hybridization using the polynucleotide as a nucleic acid probe or by quantitative RT-PCR using the polynucleotide as a primer; and

(c) a step of evaluating the presence or absence of liver cancer (or liver cancer-derived gene expression) on the basis of the measurement results of the step (b).

For example, various hybridization methods can be used for detecting, examining, evaluating, or diagnosing liver cancer (or liver cancer-derived gene expression) in vitro according to the present invention. For example, Northern blot, Southern blot, RT-PCR, DNA chip analysis, in situ hybridization, Northern hybridization, or Southern hybridization can be used as such a hybridization method.

In the case of using the Northern blot, the presence or absence of expression of each gene or the expression level thereof in the RNA can be detected or measured by use of the nucleic acid probe that can be used in the present invention. Specific examples thereof can include a method which comprises labeling the nucleic acid probe (a complementary strand) with a radioisotope (^{32}P, ^{33}P, ^{35}S, etc.), a fluorescent material, or the like, hybridizing the labeled product with the living tissue-derived RNA from the subject, which is transferred to a nylon membrane or the like according to a routine method, and then detecting and measuring a signal derived from the label (radioisotope or fluorescent material) on the formed DNA/RNA duplex using a radiation detector (examples thereof can include BAS-1800 II (Fujifilm Corp.)) or a fluorescence detector (examples thereof can include STORM 865 (GE Healthcare Japan Corp.)).

In the case of using the quantitative RT-PCR, the presence or absence of expression of each gene or the expression level thereof in the RNA can be detected or measured by use of the primer that can be used in the present invention. Specific examples thereof can include a method which comprises preparing cDNA from the living tissue-derived RNA of the subject according to a routine method, hybridizing a pair of primers (consisting of a plus strand and a reverse strand binding to the cDNA) of the present invention with the cDNA such that the region of each target gene can be amplified with the cDNA as a template, and performing PCR according to a routine method to detect the obtained double-stranded DNA. The method for detecting the double-stranded DNA can include a method of performing the PCR using the primers labeled in advance with a radioisotope or a fluorescent material, a method of electrophoresing the PCR product on an agarose gel and staining the double-stranded DNA with ethidium bromide or the like for detection, and a method of transferring the produced double-stranded DNA to a nylon membrane or the like according to a routine method and hybridizing the double-stranded DNA to a labeled nucleic acid probe for detection.

In the case of using the nucleic acid array analysis, an RNA chip or a DNA chip in which the nucleic acid probes (single-stranded or double-stranded) of the present invention are attached to a substrate (solid phase) is used. Regions having the attached nucleic acid probes are referred to as probe spots, and regions having no attached nucleic acid probe are referred to as blank spots. A group of genes immobilized on a solid-phase substrate is generally called a nucleic acid chip, a nucleic acid array, a microarray, or the like. The DNA or RNA array includes a DNA or RNA macroarray and a DNA or RNA microarray. The term "chip" used herein includes all of them. 3D-Gene® Human miRNA Oligo chip (Toray Industries, Inc.) can be used as the DNA chip, though the DNA chip is not limited thereto.

Examples of the measurement using the DNA chip can include, but are not limited to, a method of detecting and measuring a signal derived from the label on the nucleic acid probes using an image detector (examples thereof can include Typhoon 9410 (GE Healthcare Japan Corp.) and 3D-Gene® scanner (Toray Industries, Inc.)).

The "stringent conditions" used herein are, as mentioned above, conditions under which a nucleic acid probe hybridizes to its target sequence to a larger extent (e.g., a measurement value equal to or larger than a mean of background measurement values+a standard deviation of the background measurement values×2) than that for other sequences.

The stringent conditions are defined by hybridization and subsequent washing conditions. Examples of the hybridization conditions include, but not limited to, 30° C. to 60° C. for 1 to 24 hours in a solution containing SSC, a surfactant, formamide, dextran sulfate, a blocking agent, etc. In this context, 1×SSC is an aqueous solution (pH 7.0) containing 150 mM sodium chloride and 15 mM sodium citrate. The surfactant includes, for example, SDS (sodium dodecyl sulfate), Triton, or Tween. The hybridization conditions more preferably comprise 3 to 10×SSC and 0.1 to 1% SDS. Examples of the conditions for the washing, following the hybridization, which is another condition to define the stringent conditions, can include conditions comprising continuous washing at 30° C. in a solution containing 0.5×SSC and 0.1% SDS, at 30° C. in a solution containing 0.2×SSC and 0.1% SDS, and at 30° C. in a 0.05×SSC solution. It is desirable that the complementary strand should maintain its hybridized state with a target plus strand even by washing under such conditions. Specifically, examples of such a complementary strand can include a strand consisting of a nucleotide sequence in a completely complementary relationship with the nucleotide sequence of the target plus strand, and a strand consisting of a nucleotide sequence having at least 80%, preferably at least 85%, more preferably at least 90% or at least 95%, for example, at least 98% or at least 99% identity to the strand.

Other examples of the "stringent conditions" for the hybridization are described in, for example, Sambrook, J. & Russel, D., Molecular Cloning, A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press, published on Jan. 15, 2001, Vol. 1, 7.42 to 7.45 and Vol. 2, 8.9 to 8.17, and can be used in the present invention.

Examples of the conditions for carrying out PCR using a polynucleotide fragment in the kit of the present invention as a primer include treatment for approximately 15 seconds to 1 minute at 5 to 10° C. plus a Tm value calculated from the sequence of the primer, using a PCR buffer with composition such as 10 mM Tris-HCL (pH 8.3), 50 mM KCL, and 1 to 2 mM $MgCl_2$. Examples of the method for calculating such a Tm value include Tm value=2×(the number of adenine residues+the number of thymine residues)+4×(the number of guanine residues+the number of cytosine residues).

In the case of using the quantitative RT-PCR, a commercially available kit for measurement specially designed for quantitatively measuring miRNA, such as TaqMan® MicroRNA Assays (Life Technologies Corp.); LNA®-based MicroRNA PCR (Exiqon); or Ncode® miRNA qRT-PCT kit (Invitrogen Corp.) may be used.

For the calculation of gene expression levels, statistical treatment described in, for example, Statistical analysis of gene expression microarray data (Speed T., Chapman and Hall/CRC), and A beginner's guide Microarray gene expression data analysis (Causton H. C. et al., Blackwell publishing) can be used in the present invention, though the calculation method is not limited thereto. For example, twice, preferably 3 times, more preferably 6 times the standard deviation of the measurement values of the blank spots are added to the average measurement value of the blank spots on the DNA chip, and probe spots having a signal value equal to or larger than the resulting value can be regarded as detection spots. Alternatively, the average measurement value of the blank spots is regarded as a background and can be subtracted from the measurement values of the probe spots to determine gene expression levels. A missing value for a gene expression level can be excluded from the analyte, preferably replaced with the smallest value of the gene expression level in each DNA chip, or more preferably replaced with a value obtained by subtracting 0.1 from a logarithmic value of the smallest value of the gene expression level. In order to eliminate low-signal genes, only a gene having a gene expression level of 2^6, preferably 2^8, more preferably 2^{10} or larger in 20% or more, preferably 50% or more, more preferably 80% or more of the number of measurement samples can be selected as the analyte. Examples of the normalization of the gene expression level include, but are not limited to, global normalization and quantile normalization (Bolstad, B. M. et al., 2003, Bioinformatics, Vol. 19, p. 185-193).

The present invention also provides a method comprising measuring a target gene or gene expression level in a sample derived from a subject using the polynucleotide, the kit, or the device (e.g., chip) for detection of the present invention, or a combination thereof, preparing a discriminant (discriminant function) with gene expression levels in a sample derived from a liver cancer patient and a sample derived from a healthy subject as supervising samples, and determining or evaluating the presence and/or absence of the liver cancer-derived gene in the sample.

Specifically, the present invention further provides the method comprising: a first step of measuring in vitro an expression level of a target gene (target nucleic acids) in multiple samples known to determine or evaluate the presence or absence of the liver cancer-derived gene in the samples, using the polynucleotide, the kit, or the device (e.g., chip) for detection of the present invention, or a combination thereof; a second step of constructing a discriminant with the measurement values of the expression level of the target gene obtained in the first step as supervising samples; a third step of measuring in vitro an expression level of the target gene in a sample derived from a subject in the same way as in the first step; and a fourth step of substituting the measurement value of the expression level of the target gene obtained in the third step into the discriminant obtained in the second step, and determining or evaluating the presence or absence of the liver cancer-derived gene in the sample on the basis of the results obtained from the discriminant, wherein the target gene can be detected using the polynucleotide or using a polynucleotide for detection contained in the kit or the device (e.g., chip). In this context, the discriminant can be prepared by use of Fisher's linear discriminant analysis, nonlinear discriminant analysis based on Mahalanobis' distance, neural network, Support Vector Machine (SVM), or the like, though the method is not limited thereto.

When a clustering boundary is a straight line or a hyperplane, the linear discriminant analysis is a method for determining the association of a cluster using Formula 1 as a discriminant. In this formula, x represents an explanatory variable, w represents a coefficient of the explanatory variable, and w_0 represents a constant term.

$$f(x) = w_0 + \sum_{i=1}^{n} w_i x_i \qquad \text{Formula 1}$$

Values obtained from the discriminant are referred to as discriminant scores. The measurement values of a newly

offered data set can be substituted as explanatory variables into the discriminant to determine clusters on the basis of the signs of the discriminant scores.

The Fisher's linear discriminant analysis, one type of linear discriminant analysis, is a dimensionality reduction method for selecting a dimension suitable for discriminating classes, and constructs a highly discriminating synthetic variable by focusing on the variance of the synthetic variables and minimizing the variance of data having the same label (Venables, W. N. et al., Modern Applied Statistics with S. Fourth edition. Springer., 2002). In the Fisher's linear discriminant analysis, direction w of projection is determined so as to maximize Formula 2. In this formula, μ represents an average input, ng represents the number of data associated with class g, and μg represents an average input of the data associated with class g. The numerator and the denominator are interclass variance and intraclass variance, respectively, when each data is projected in the direction of the vector w. Discriminant coefficient wi is determined by maximizing this ratio (Takafumi Kanamori et al., "Pattern Recognition", Kyoritsu Shuppan Co., Ltd. (2009); and Richard O. et al., Pattern Classification Second Edition., Wiley-Interscience, 2000).

$$J(w) = \frac{\sum_{g=1}^{G} n_g (w^T \mu_g - w^T \mu)(w^T \mu_g - w^T \mu)^T}{\sum_{g=1}^{G} \sum_{i:\, y_i = g} (w^T x_i - w^T \mu_g)(w^T x_i - w^T \mu_g)} \quad \text{Formula 2}$$

$$\text{subject to } \mu = \sum_{i=1}^{n} \frac{x_i}{n}, \mu_g = \sum_{i:\, u_i = g}^{n} \frac{x_i}{n_g}$$

The Mahalanobis' distance is calculated according to Formula 3 in consideration of data correlation and can be used as nonlinear discriminant analysis for determining an associated cluster, based on a closer Mahalanobis' distance from each cluster. In this Formula 3, μ represents a central vector of each cluster, and S^{-1} represents an inverse matrix of the variance-covariance matrix of the cluster. The central vector is calculated from explanatory variable x, and an average vector, a median value vector, or the like can be used.

$$D(x, \mu) = \{(x - \mu)^t S^{-1} (x - \mu)\}^{\frac{1}{2}} \quad \text{Formula 3}$$

SVM is a discriminant analysis method devised by V. Vapnik (The Nature of Statistical Leaning Theory, Springer, 1995). Particular data points of a data set having known classes are defined as explanatory variables, and classes are defined as objective variables. A boundary plane called hyperplane for correctly classifying the data set into the known classes is determined, and a discriminant for data classification is determined using the boundary plane. Then, the measurement values of a newly offered data set can be substituted as explanatory variables into the discriminant to determine classes. In this respect, the result of the discriminant analysis may be classes, may be a probability of data to be classified into correct classes, or may be the distance from the hyperplane. In SVM, a method of nonlinearly converting a feature vector to a high dimension and performing linear discriminant analysis in the space is known as a method for tackling nonlinear problems. A formula in which an inner product of two factors in a nonlinearly mapped space is expressed only by inputs in their original spaces is called kernel. Examples of the kernel can include a linear kernel, a RBF (radial basis function) kernel, and a Gaussian kernel. While highly dimensional mapping is performed according to the kernel, the optimum discriminant, i.e., a discriminant, can be actually constructed by mere calculation according to the kernel, which avoids calculating features in the mapped space (e.g., Hideki Aso et al., Frontier of Statistical Science 6 "Statistics of pattern recognition and learning—New concepts and approaches", Iwanami Shoten, Publishers (2004); Nello Cristianini et al., Introduction to SVM, Kyoritsu Shuppan Co., Ltd. (2008)).

C-support vector classification (C-SVC), one type of SVM, comprises preparing a hyperplane by supervising with the explanatory variables of two groups and classifying an unknown data set into either of the groups (C. Cortes et al., 1995, Machine Learning, Vol. 20, p. 273-297).

Exemplary calculation of the C-SVC discriminant that can be used in the method of the present invention will be given below. First, all subjects are divided into two groups, i.e., a liver cancer patient group and a healthy subject group. For example, liver tissue examination can be used for confirming each subject either as a liver cancer patient or as a healthy subject.

Next, a data set consisting of comprehensive gene expression levels of serum-derived samples of the two divided groups (hereinafter, this data set is referred to as a training cohort) is prepared, and a C-SVC discriminant is determined by using genes found to differ clearly in their gene expression levels between the two groups as explanatory variables and this grouping as objective variables (e.g., −1 and +1). An optimizing objective function is represented by Formula 4 wherein e represents all input vectors, y represents an objective variable, a represents a Lagrange's undetermined multiplier vector, Q represents a positive definite matrix, and C represents a parameter for adjusting constrained conditions.

$$\min_a \ \frac{1}{2} a^T Q a - e^T a \quad \text{Formula 4}$$

$$\text{subject to } y^T a = 0, 0 \le a_i \le C, i = 1, \ldots, l,$$

Formula 5 is a finally obtained discriminant, and a group to which the data point is associated can be determined on the basis of the sign of a value obtained according to the discriminant. In this formula, x represents a support vector, y represents a label indicating the association of a group, a represents the corresponding coefficient, b represents a constant term, and K represents a kernel function.

$$f(x) = \mathrm{sgn}\left(\sum_{i=1}^{l} y_i a_i K(x_i, x) + b\right) \quad \text{Formula 5}$$

For example, a RBF kernel defined by Formula 6 can be used as the kernel function. In this formula, x represents a support vector, and γ represents a kernel parameter for adjusting the complexity of the hyperplane.

$$K(x_i, x_j) = \exp(-r\|x_i - x_j\|^2), r < 0 \quad \text{Formula 6}$$

In addition, an approach such as neural network, k-nearest neighbor algorithms, decision trees, or logistic regression analysis can be selected as a method for determining or

evaluating the presence and/or absence of expression of a liver cancer-derived target gene in a sample derived from a subject, or for evaluating the expression level thereof by comparison with a control derived from a healthy subject.

The method of the present invention can comprise, for example, the following steps (a), (b), and (c):

(a) measuring an expression level of a target gene in tissues containing liver cancer-derived genes derived from liver cancer patients and/or samples that are already known to contain no liver cancer-derived gene derived from healthy subjects, using the polynucleotide, the kit, or the device (e.g., DNA chip) for detection according to the present invention;

(b) preparing the discriminants of Formulae 1 to 3, 5, and 6 described above from the measurement values of the expression level measured in the step (a); and

(c) measuring an expression level of the target gene in a sample derived from a subject using the polynucleotide, the kit, or the device (e.g., DNA chip) for detection according to the present invention, substituting the obtained measurement value into the discriminants prepared in the step (b), and determining or evaluating the presence and/or absence of the liver cancer-derived target gene in the sample, or evaluating the expression level thereof by comparison with a healthy subject-derived control, on the basis of the obtained results.

In this context, in the discriminants of Formulae 1 to 3, 5, and 6, x represents an explanatory variable and includes a value obtained by measuring a polynucleotide selected from the polynucleotides described above in the Section 2, or a fragment thereof, etc. Specifically, the explanatory variable for discriminating a liver cancer patient from a healthy subject according to the present invention is a gene expression level selected from, for example, the following expression levels (1) to (3):

(1) a gene expression level in the serum of a pancreatic cancer patient or a healthy subject measured by any of DNA comprising 15 or more consecutive nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a complementary sequence thereof,

(2) a gene expression level in the serum of a pancreatic cancer patient or a healthy subject measured by any of DNA comprising 15 or more consecutive nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a complementary sequence thereof, and

(3) a gene expression level in the serum of a liver cancer patient or a healthy subject measured by any DNA comprising 15 or more consecutive nucleotides in a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a complementary sequence thereof.

As described above, for the method for determining or evaluating the presence and/or absence of a liver cancer-derived gene in a sample derived from a subject, the preparation of a discriminant requires a discriminant prepared in a training cohort. For enhancing the discriminant accuracy of the discriminant, it is necessary for the discriminant to use genes that show clear difference between two groups in the training cohort when preparing the discriminant.

Each gene that is used for an explanatory variable in a discriminant is preferably determined as follows. First, comprehensive gene expression levels of a liver cancer patient group and comprehensive gene expression levels of a healthy subject group, both of which are in a training cohort, are used as a data set, the degree of difference in the expression level of each gene between the two groups is determined through the use of, for example, the P value of t test, which is parametric analysis, or the P value of Mann-Whitney's U test or Wilcoxon test, which is nonparametric analysis.

The gene can be regarded as being statistically significant when the critical rate (significance level) as the P value obtained by the test is smaller than, for example, 5%, 1%, or 0.01%.

In order to correct an increased probability of type I error attributed to the repetition of a test, a method known in the art, for example, Bonferroni or Holm method, can be used for the correction (e.g., Yasushi Nagata et al., "Basics of statistical multiple comparison methods", Scientist Press Co., Ltd. (2007)). As an example of the Bonferroni correction, for example, the P value obtained by a test is multiplied by the number of repetitions of the test, i.e., the number of genes used in the analysis, and the obtained value can be compared with a desired significance level to suppress a probability of causing type I error in the whole test.

Instead of the statistical test, the absolute value (fold change) of an expression ratio of a median value of each gene expression level between gene expression levels of a liver cancer patient group and gene expression levels of a healthy subject group may be calculated to select a gene that is used for an explanatory variable in a discriminant. Alternatively, ROC curves may be prepared using gene expression levels of a liver cancer patient group and a healthy subject group, and a gene that is used for an explanatory variable in a discriminant can be selected on the basis of an AUROC value.

Next, a discriminant that can be calculated by various methods described above is prepared using any number of genes having large difference in their gene expression levels determined here. Examples of the method for constructing a discriminant that produces the largest discriminant accuracy include a method of constructing a discriminant in every combination of genes that satisfy the significance level of P value, and a method of repetitively evaluating the genes for use in the preparation of a discriminant while increasing the number of genes one by one in a descending order of difference in gene expression level (Furey T S. et al., 2000, Bioinformatics., Vol. 16, p. 906-14). A gene expression level of another independent liver cancer patient or healthy subject is substituted as an explanatory variable into this discriminant to calculate discrimination results of the group to which this independent liver cancer patient or healthy subject belongs. Specifically, the found gene set for diagnosis and the discriminant constructed using the gene set for diagnosis can be evaluated in an independent sample cohort to find a more universal gene set for diagnosis capable of detecting liver cancer and a more universal method for discriminating liver cancer.

Split-sample method is preferably used for evaluating the discriminant performance (generality) of the discriminant. Specifically, a data set is divided into a training cohort and a validation cohort, and gene selection by a statistical test and discriminant preparation are performed using the training cohort. Accuracy, sensitivity, and specificity are calculated using results of discriminating a validation cohort according to the discriminant and a true group to which the validation cohort associates, to evaluate the discriminant performance. On the other hand, instead of dividing a data set, the gene selection by a statistical test and discriminant preparation may be performed using all of samples, and accuracy, sensitivity, and specificity can be calculated by the discriminant analysis using a newly prepared samples cohort for evaluation of the discriminant performance.

The present invention provides a polynucleotide for detection or for disease diagnosis useful in the diagnosis and treatment of liver cancer, a method for detecting liver cancer using the polynucleotide, and a kit and a device for the detection of liver cancer, comprising the polynucleotide. Particularly, in order to select a gene for diagnosis and prepare a discriminant so as to exhibit accuracy beyond a liver cancer diagnosis method using an existing tumor marker CEA, a gene set for diagnosis and a discriminant for the method of the present invention, that exhibit accuracy beyond AFP, CEA, CA19-9 and/or PIVKA-II, can be constructed, for example, by comparing expressed genes in serum derived from a patient confirmed to be negative using AFP, CEA, CA19-9, and/or PIVKA-II but finally found to have liver cancer by detailed examination such as computed tomography using a contrast medium, with genes expressed in serum derived from a patient having no liver cancer.

For example, the gene set for diagnosis is set to any combination selected from one or two or more of the polynucleotides based on a nucleotide sequence represented by any of SEQ ID NOs: 1 to 167 and 714 to 729 or a complementary sequence thereof as described above, optionally one or two or more of the polynucleotides based on a nucleotide sequence represented by any of SEQ ID NOs: 168 to 183 or a complementary sequence thereof, and optionally one or two or more of the polynucleotides based on a nucleotide sequence represented by any of SEQ ID NOs: 184 to 224 or a complementary sequence thereof. Further, a discriminant is constructed using expression levels of the gene set for diagnosis in samples derived from class I liver cancer patients as a result of tissue diagnosis and samples derived from class II healthy subjects as a result of tissue diagnosis. As a result, the presence or absence of liver cancer-derived genes in an unknown sample can be determined with 100% accuracy at the maximum by measuring expression levels of the gene set for diagnosis in an unknown sample.

EXAMPLES

Hereinafter, the present invention is described further specifically with reference to Examples below. However, the scope of the present invention is not intended to be limited by these Examples.

Reference Example 1

Collection of Samples from Liver Cancer Patients and Healthy Subjects

Sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from 100 healthy subjects and 34 liver cancer patients (15 cases with stage I, 9 cases with stage II, 5 cases with stage IIIA, 2 cases with stage IIIB, 1 case with stage IIIC, and 2 cases with stage IV) confirmed to have no primary cancer other than liver cancer after acquisition of informed consent, and used as a training cohort. Likewise, sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from 50 healthy subjects and 16 liver cancer patients (9 cases with stage I, 5 cases with stage II, and 2 cases with stage IIIA) confirmed to have no primary cancer other than liver cancer after acquisition of informed consent, and used as a validation cohort.

Extraction of Total RNA

Total RNA was obtained from 300 μL of the serum sample obtained from each of 200 persons in total of 150 healthy subjects and 50 liver cancer patients included in the training cohort and the validation cohort, using a reagent for RNA extraction in 3D-Gene® RNA extraction reagent from liquid sample kit (Toray Industries, Inc.) according to the protocol provided by the manufacturer.

Measurement of Gene Expression Level

miRNAs in the total RNA obtained from the serum sample of each of 200 persons in total of 150 healthy subjects and 50 liver cancer patients included in the training cohort and the validation cohort were fluorescently labeled using 3D-Gene® miRNA Labeling kit (Toray Industries, Inc.) according to the protocol (ver 2.20) provided by the manufacturer. The oligo DNA chip used was 3D-Gene® Human miRNA Oligo chip (Toray Industries, Inc.) with attached probes having sequences complementary to 2,555 miRNAs among the miRNAs registered in miRBase Release 20. Hybridization between the miRNAs in the total RNA and the probes on the DNA chip under stringent conditions and washing following the hybridization were performed according to the protocol provided by the manufacturer. The DNA chip was scanned using 3D-Gene® scanner (Toray Industries, Inc.) to obtain images. Fluorescence intensity was digitized using 3D-Gene® Extraction (Toray Industries, Inc.). The digitized fluorescence intensity was converted to a logarithmic value having a base of 2 and used as a gene expression level, from which a blank value was subtracted. A missing value was replaced with a value obtained by subtracting 0.1 from a logarithmic value of the smallest value of the gene expression level in each DNA chip. As a result, the comprehensive gene expression levels of the miRNAs in the sera were obtained for the 150 liver cancer patients and the 150 healthy subjects. Calculation and statistical analysis using the digitized gene expression levels of the miRNAs were carried out using R language 3.0.2 (R Development Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, URL http://www.R-project.org/.) and MASS package 7.3-30 (Venables, W. N. & Ripley, B. D. (2002) Modern Applied Statistics with S. Fourth Edition. Springer, New York. ISBN 0-387-95457-0).

Reference Example 2

Collection of Samples from Patients with Cancers Other than Liver Cancer

Sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 72 pancreatic cancer patients, 61 bile duct cancer patients, 38 stomach cancer patients, 25 esophageal cancer patients, 35 colorectal cancer patients, and 16 benign pancreaticobiliary disease patients confirmed to have no cancer in other organs after acquisition of informed consent, and used as a training cohort together with the samples of 35 liver cancer patients and 99 healthy subjects of Reference Example 1. Likewise, sera were collected using VENOJECT II vacuum blood collecting tube VP-AS109K60 (Terumo Corp.) from each of 28 pancreatic cancer patients, 37 bile duct cancer patients, 12 stomach cancer patients, 25 esophageal cancer patients, 15 colorectal cancer patients, and 5 benign pancreaticobiliary disease patients confirmed to have no cancer in other organs after acquisition of informed consent, and used as a validation cohort together with the samples of 17 liver cancer patients confirmed to have no cancer in organs except for liver cancer and 51 healthy subjects of Reference

Example 1. Subsequent operations were conducted in the same way as in Reference Example 1.

Example 1

Selection of Gene Marker Using Samples in the Training Cohort, and Method for Evaluating Liver Cancer Discriminant Performance of the Single Gene Marker Using Samples in the Validation Cohort

In this Example, a gene marker for discriminating a liver cancer patient from a healthy subject was selected from the training cohort, and studied in samples of the validation cohort independent of the training cohort, for a method for evaluating liver cancer discriminant performance of each selected gene marker alone.

Specifically, first, the miRNA expression levels in the training cohort and the validation cohort obtained in the above-mentioned Reference Examples were combined and normalized by quantile normalization.

Next, genes for diagnosis were selected in the training cohort. Here, in order to acquire diagnostic markers with higher reliability, only genes having the gene expression level of 2^6 or higher in 50% or more of the samples in either of the liver cancer patient group in the training cohort or the healthy subject group of the training cohort were selected. In order to further acquire statistically significant genes for discriminating a liver cancer patient group from a healthy subject group, the P value obtained by two-tailed t-test assuming equal variance as to each gene expression level was corrected by the Bonferroni method, and genes that satisfied $p<0.01$ were acquired as gene markers for use in explanatory variables of a discriminant and described in Table 2.

In this way, hsa-miR-1343-3p, hsa-miR-6726-5p, hsa-miR-6515-3p, hsa-miR-4651, hsa-miR-4257, hsa-miR-3188, hsa-miR-6131, hsa-miR-6766-3p, hsa-miR-7641, hsa-miR-1249, hsa-miR-3679-3p, hsa-miR-6787-5p, hsa-miR-4454, hsa-miR-3135b, hsa-miR-6765-3p, hsa-miR-7975, hsa-miR-204-3p, hsa-miR-7977, hsa-miR-7110-5p, hsa-miR-6717-5p, hsa-miR-6870-5p, hsa-miR-663b, hsa-miR-6875-5p, hsa-miR-8072, hsa-miR-6816-5p, hsa-miR-4281, hsa-miR-6729-5p, hsa-miR-8069, hsa-miR-4706, hsa-miR-7108-5p, hsa-miR-4433b-3p, hsa-miR-6893-5p, hsa-miR-6857-5p, hsa-miR-1227-5p, hsa-miR-6741-5p, hsa-miR-451a, hsa-miR-8063, hsa-miR-3622a-5p, hsa-miR-615-5p, hsa-miR-128-1-5p, hsa-miR-6825-5p, hsa-miR-1260b, hsa-miR-4433-3p, hsa-miR-4665-5p, hsa-miR-7845-5p, hsa-miR-1908-5p, hsa-miR-6840-3p, hsa-miR-6765-5p, hsa-miR-296-5p, hsa-miR-3675-3p, hsa-miR-6781-5p, hsa-miR-423-5p, hsa-miR-3663-3p, hsa-miR-6784-5p, hsa-miR-6749-5p, hsa-miR-1231, hsa-miR-4746-3p, hsa-miR-6780b-5p, hsa-miR-4758-5p, hsa-miR-3679-5p, hsa-miR-3184-5p, hsa-miR-6125, hsa-miR-6721-5p, hsa-miR-6791-5p, hsa-miR-3185, hsa-miR-1260a, hsa-miR-3197, hsa-miR-6845-5p, hsa-miR-6887-5p, hsa-miR-6738-5p, hsa-miR-6872-3p, hsa-miR-4497, hsa-miR-1229-5p, hsa-miR-6820-5p, hsa-miR-6777-5p, hsa-miR-3917, hsa-miR-5787, hsa-miR-4286, hsa-miR-6877-5p, hsa-miR-1225-3p, hsa-miR-6088, hsa-miR-6800-5p, hsa-miR-1246, hsa-miR-4467, hsa-miR-4419b, hsa-miR-1914-3p, hsa-miR-4632-5p, hsa-miR-1915-5p, hsa-miR-3940-5p, hsa-miR-1185-2-3p, hsa-miR-6746-5p, hsa-miR-5001-5p, hsa-miR-1228-5p, hsa-miR-5572, hsa-miR-4327, hsa-miR-4638-5p, hsa-miR-6799-5p, hsa-miR-6861-5p, hsa-miR-6727-5p, hsa-miR-4513, hsa-miR-6805-3p, hsa-miR-6808-5p, hsa-miR-4449, hsa-miR-1199-5p, hsa-miR-1275, hsa-miR-4792, hsa-miR-4443, hsa-miR-6891-5p, hsa-miR-6826-5p, hsa-miR-6807-5p, hsa-miR-7150, hsa-miR-4534, hsa-miR-4476, hsa-miR-4649-5p, hsa-miR-4525, hsa-miR-1915-3p, hsa-miR-4516, hsa-miR-4417, hsa-miR-642b-3p, hsa-miR-3141, hsa-miR-5100, hsa-miR-6848-5p, hsa-miR-4739, hsa-miR-4459, hsa-miR-1237-5p, hsa-miR-296-3p, hsa-miR-4665-3p, hsa-miR-6786-5p, hsa-miR-4258, hsa-miR-6510-5p, hsa-miR-1343-5p, hsa-miR-1247-3p, hsa-miR-6805-5p, hsa-miR-4492, hsa-miR-1469, hsa-miR-1268b, hsa-miR-6858-5p, hsa-miR-3937, hsa-miR-939-5p, hsa-miR-3656, hsa-miR-744-5p, hsa-miR-4687-3p, hsa-miR-4763-3p, hsa-miR-3620-5p, hsa-miR-3195, hsa-miR-6842-5p, hsa-miR-4707-5p, hsa-miR-642a-3p, hsa-miR-7113-3p, hsa-miR-4728-5p, hsa-miR-5195-3p, hsa-miR-1185-1-3p, hsa-miR-6774-5p, hsa-miR-8059, hsa-miR-3131, hsa-miR-7847-3p, hsa-miR-4463, hsa-miR-128-2-5p, hsa-miR-4508, hsa-miR-6806-5p, hsa-miR-7111-5p, hsa-miR-6782-5p, hsa-miR-4734, hsa-miR-3162-5p, hsa-miR-887-3p, hsa-miR-6752-5p, hsa-miR-6724-5p, hsa-miR-23b-3p, hsa-miR-23a-3p, hsa-miR-625-3p, hsa-miR-1228-3p, hsa-miR-614, hsa-miR-1913, hsa-miR-92a-2-5p, hsa-miR-187-5p, hsa-miR-16-5p, hsa-miR-92b-3p, hsa-miR-150-3p, hsa-miR-564, hsa-miR-125a-3p, hsa-miR-92b-5p, hsa-miR-92a-3p, and hsa-miR-663a genes represented by SEQ ID NOs: 1 to 183 were found as liver cancer markers relative to the healthy subjects.

Among them, genes newly found as markers for examining the presence or absence of liver cancer are polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 167.

A discriminant for determining the presence or absence of liver cancer was further prepared by Fisher's linear discriminant analysis with the expression levels of these genes as an indicator. Specifically, any newly found polynucleotide consisting of a nucleotide sequence represented by any of SEQ ID NOs: 1 to 183 in the training cohort was input to Formula 2 to construct a discriminant. Calculated accuracy, sensitivity, and specificity are shown in Table 3. In this respect, a discriminant coefficient and a constant term are shown in Table 4.

Accuracy, sensitivity, and specificity in the validation cohort were calculated using the discriminant thus prepared, and the discriminant performance of the selected polynucleotides was validated using independent samples (Table 3). For example, the expression level measurement value of the nucleotide sequence represented by SEQ ID NO: 1 was compared between the healthy subjects (100 persons) and the liver cancer patients (34 persons) in the training cohort. As a result, the gene expression level measurement values were found to be significantly lower in the liver cancer patient group than in the healthy subject group (see the left diagram of FIG. **2**). These results were also reproducible for the healthy subjects (50 persons) and the liver cancer patients (16 persons) in the validation cohort (see the right diagram of FIG. **2**). Likewise, the results obtained about the other polynucleotides shown in SEQ ID NOs: 2 to 183 showed that the gene expression level measurement values were significantly lower (−) or higher (+) in the liver cancer patient group than in the healthy subject group (Table 2). These results were able to be validated in the validation cohort. For example, as for this nucleotide sequence represented by SEQ ID NO: 1, the number of samples that were correctly identified in the detection of liver cancer was calculated using the threshold (7.09) that was set in the training cohort and discriminated between the two groups. As a result, 15 true positives, 49 true negatives, 1 false

positive, and 1 false negatives were obtained in the validation cohort. From these values, 97% accuracy, 94% sensitivity, and 98% specificity were obtained as the detection performance. In this way, the detection performance was calculated as to all of the polynucleotides shown in SEQ ID NOs: 1 to 183, and described in Table 3.

Likewise, 72 polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 33, 34, 35, 37, 39, 40, 41, 43, 44, 45, 46, 47, 48, 50, 51, 54, 55, 56, 57, 58, 60, 61, 62, 63, 64, 65, 68, 73, 80, 86, 88, 91, 93, 94, 99, 114, 117, 170, 171, 172, 173, 174 and 175 exhibited sensitivity of 93.8%, 93.8%, 93.8%, 87.5%, 75%, 87.5%, 62.5%, 81.2%, 93.8%, 93.8%, 75%, 93.8%, 62.5%, 93.8%, 56.2%, 56.2%, 56.2%, 93.8%, 68.8%, 87.5%, 93.8%, 81.2%, 87.5%, 62.5%, 56.2%, 68.8%, 81.2%, 81.2%, 62.5%, 87.5%, 68.8%, 75%, 75%, 75%, 62.5%, 93.8%, 75%, 56.2%, 62.5%, 62.5%, 68.8%, 87.5%, 75%, 62.5%, 75%, 68.8%, 62.5%, 68.8%, 68.8%, 68.8%, 62.5%, 62.5%, 75%, 62.5%, 75%, 68.8%, 56.2%, 81.2%, 68.8%, 56.2%, 62.5%, 56.2%, 56.2%, 68.8%, 56.2%, 62.5%, 87.5%, 87.5%, 75%, 68.8%, 62.5% and 81.2% respectively, in the validation cohort (Table 3). As seen from Comparative Example mentioned later, AFP, which had the highest sensitivity among four existing markers, had sensitivity of 53.3% in the validation cohort (Table 5), demonstrating that, for example, the 72 polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 33, 34, 35, 37, 39, 40, 41, 43, 44, 45, 46, 47, 48, 50, 51, 54, 55, 56, 57, 58, 60, 61, 62, 63, 64, 65, 68, 73, 80, 86, 88, 91, 93, 94, 99, 114, 117, 170, 171, 172, 173, 174 and 175 can discriminate, each alone, liver cancer in the validation cohort with sensitivity beyond AFP.

Also, for example, 7 polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 6, 15, 31, 46, 50, and 58 were able to correctly determine all of the nine stage 1 liver cancer samples contained in the validation cohort to have liver cancer. Thus, these polynucleotides can detect even early liver cancer and contribute to the early diagnosis of liver cancer.

Example 2

Method for Evaluating Liver Cancer Discriminant Performance by Combination of Multiple Gene Markers Using Samples in the Validation Cohort

In this Example, a method for evaluating liver cancer discriminant performance by a combination of the gene markers selected in Example 1 was studied. Specifically, Fisher's linear discriminant analysis was conducted as to 16,533 combinations of two expression level measurement values comprising at least one or more of the expression level measurement values of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 167 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183 selected in Example 1, to construct a discriminant for determining the presence or absence of liver cancer. Next, accuracy, sensitivity, and specificity in the validation cohort were calculated using the discriminant thus prepared, and the discriminant performance of the selected polynucleotides was validated using the independent samples.

For example, the expression level measurement values of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NO: 1 and SEQ ID NO: 2 were compared between the healthy subjects (100 persons) and the liver cancer patients (34 persons) in the training cohort. As a result, a scatter diagram that significantly separated the expression level measurement values of the liver cancer patient group from those of the healthy subject group was obtained (see the left diagram of FIG. **3**). These results were also reproducible for the healthy subjects (50 persons) and the liver cancer patients (16 persons) in the validation cohort (see the right diagram of FIG. **3**). Likewise, a scatter diagram that significantly separated the expression level measurement values of the liver cancer patient group from those of the healthy subject group was also obtained as to the other combinations of two expression level measurement values comprising at least one or more of the expression level measurement values of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 167 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183. These results were able to be validated in the validation cohort. For example, as for these nucleotide sequences represented by SEQ ID NO: 1 and SEQ ID NO: 2, the number of correctly or incorrectly identified samples in the detection of liver cancer was calculated using the function (0=0.77x+y−15.07) that was set in the training cohort and discriminated between the two groups. As a result, 16 true positives, 50 true negatives, 0 false positives, and 0 false negatives were obtained. From these values, 100% accuracy, 100% sensitivity, and 100% specificity were obtained as the detection performance. In this way, the detection performance was calculated for all combinations of two expression level measurement values comprising at least one more of the expression level measurement values of any of the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 167 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183. Among them, 182 combinations comprising the expression level measurement value of the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 and the detection performance thereof were described in Table 6 as an example. For example, all of combinations of the expression level measurement values of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 and 2, SEQ ID NOs: 1 and 3, SEQ ID NOs: 1 and 4, and SEQ ID NOs: 1 and 5 exhibited sensitivity of 100%, 100%, 100%, 94%, and 94%, respectively, in the validation cohort. Likewise, the sensitivity was also calculated as to the combinations of two polynucleotides consisting of the nucleotide sequences represented by SEQ ID NO: 1 and any of SEQ ID NOs: 6 to 251. As a result, all of these combinations exhibited sensitivity of 88% or higher (Table 6), which was beyond the sensitivity (53.3%) of the existing liver cancer marker AFP (Table 5). Thus, a combination of two of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183 also produced excellent liver cancer detection sensitivity.

In addition, markers for the detection of liver cancer with more excellent sensitivity are obtained by combining the expression level measurement values of 3, 4, 5, 6, 7, 8, 9, 10 or more of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183. For example, the newly found polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 167 among the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183 selected in Example 1 were measured to obtain their expression levels

of the healthy subject group and the liver cancer group in the validation cohort. All of the polynucleotides were ranked in the descending order of their P values based on the Student's t-test which indicate statistical significance of difference between groups (i.e., one having the lowest P value was ranked in the first place), and liver cancer detection sensitivity was evaluated for each of combinations of one or more polynucleotides to which the polynucleotides were added one by one from the top to the bottom according to the rank. In short, the order in terms of SEQ ID NOs in which the polynucleotides were combined in this evaluation is in reverse in terms of SEQ ID NO: 167 to SEQ ID NOs: 166, 165, . . . shown in Table 2 in order. As a result, the sensitivity in the validation cohort was 12.5% for 1 polynucleotide (SEQ ID NO: 167), 43.8% for 2 polynucleotides (SEQ ID NOs: 166 and 167), 68.8% for 4 polynucleotides (SEQ ID NOs: 164 to 167), 87.5% for 6 polynucleotides (SEQ ID NOs: 162 to 167), 93.8% for 10 polynucleotides (SEQ ID NOs: 158 to 167), 100% for 20 polynucleotides (SEQ ID NOs: 148 to 167), 100% for 30 polynucleotides (SEQ ID NOs: 138 to 167), 100% for 50 polynucleotides (SEQ ID NOs: 118 to 167), 100% for 80 polynucleotides (SEQ ID NOs: 88 to 167), 100% for 110 polynucleotides (SEQ ID NOs: 58 to 167), 100% for 150 polynucleotides (SEQ ID NOs: 18 to 167), and 100% for 167 polynucleotides (SEQ ID NOs: 1 to 167).

These results demonstrated that a combination of a plurality of polynucleotides can produce higher liver cancer discriminant performance than that of each polynucleotide alone or a combination of a fewer number of polynucleotides. In this context, the combinations of a plurality of polynucleotides are not limited to the combinations of the polynucleotides added in the order of statistically significant difference as described above, and any combination of a plurality of polynucleotides can be used in the detection of liver cancer.

From these results, it can be concluded that all of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183 serve as excellent markers for the detection of liver cancer.

TABLE 2

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in liver cancer patient relative to healthy subject
1	hsa-miR-1343-3p	6.65.E-37	–
2	hsa-miR-6726-5p	2.01.E-34	–
3	hsa-miR-6515-3p	4.26.E-28	+
4	hsa-miR-4651	1.83.E-27	–
5	hsa-miR-4257	5.63.E-27	–
6	hsa-miR-3188	1.06.E-25	+
7	hsa-miR-6131	4.08.E-25	–
8	hsa-miR-6766-3p	1.86.E-24	+
9	hsa-miR-7641	5.24.E-24	–
10	hsa-miR-1249	1.67.E-23	+
11	hsa-miR-3679-3p	3.33.E-23	+
12	hsa-miR-6787-5p	5.69.E-23	–
13	hsa-miR-4454	6.89.E-23	–
14	hsa-miR-3135b	3.83.E-21	–
15	hsa-miR-6765-3p	2.37.E-20	–
16	hsa-miR-7975	1.57.E-19	–
17	hsa-miR-204-3p	2.58.E-19	–
18	hsa-miR-7977	5.17.E-18	–
19	hsa-miR-7110-5p	1.34.E-16	+
20	hsa-miR-6717-5p	1.77.E-16	–
21	hsa-miR-6870-5p	1.86.E-16	+
22	hsa-miR-663b	1.91.E-16	–
23	hsa-miR-6875-5p	1.98.E-16	+
24	hsa-miR-8072	2.20.E-16	+
25	hsa-miR-6816-5p	4.02.E-16	+
26	hsa-miR-4281	1.18.E-15	–
27	hsa-miR-6729-5p	1.90.E-15	+
28	hsa-miR-8069	4.12.E-15	+
29	hsa-miR-4706	9.80.E-15	–
30	hsa-miR-7108-5p	1.34.E-14	+
31	hsa-miR-4433b-3p	1.44.E-14	+
32	hsa-miR-6893-5p	2.25.E-14	–
33	hsa-miR-6857-5p	3.37.E-14	+
34	hsa-miR-1227-5p	5.86.E-14	+
35	hsa-miR-6741-5p	1.52.E-13	–
36	hsa-miR-451a	1.99.E-13	–
37	hsa-miR-8063	2.08.E-13	–
38	hsa-miR-3622a-5p	2.29.E-13	–
39	hsa-miR-615-5p	2.47.E-13	–
40	hsa-miR-128-1-5p	6.21.E-13	+
41	hsa-miR-6825-5p	1.19.E-12	+
42	hsa-miR-1260b	2.03.E-12	–
43	hsa-miR-4433-3p	2.67.E-12	+
44	hsa-miR-4665-5p	3.11.E-12	–
45	hsa-miR-7845-5p	3.97.E-12	+
46	hsa-miR-1908-5p	4.05.E-12	+
47	hsa-miR-6840-3p	5.71.E-12	–
48	hsa-miR-6765-5p	5.84.E-12	+
49	hsa-miR-296-5p	6.23.E-12	+
50	hsa-miR-3675-3p	1.58.E-11	+
51	hsa-miR-6781-5p	5.32.E-11	+
52	hsa-miR-423-5p	5.46.E-11	–
53	hsa-miR-3663-3p	5.53.E-11	–
54	hsa-miR-6784-5p	5.78.E-11	+
55	hsa-miR-6749-5p	7.92.E-11	–
56	hsa-miR-1231	1.43.E-10	+
57	hsa-miR-4746-3p	1.47.E-10	+
58	hsa-miR-6780b-5p	1.80.E-10	+
59	hsa-miR-4758-5p	1.80.E-10	–
60	hsa-miR-3679-5p	2.45.E-10	+
61	hsa-miR-3184-5p	3.79.E-10	+
62	hsa-miR-6125	4.04.E-10	+
63	hsa-miR-6721-5p	9.40.E-10	+
64	hsa-miR-6791-5p	1.05.E-09	+
65	hsa-miR-3185	1.24.E-09	+
66	hsa-miR-1260a	1.37.E-09	–
67	hsa-miR-3197	1.86.E-09	+
68	hsa-miR-6845-5p	2.23.E-09	+
69	hsa-miR-6887-5p	2.95.E-09	–
70	hsa-miR-6738-5p	5.06.E-09	–
71	hsa-miR-6872-3p	5.23.E-09	–
72	hsa-miR-4497	5.30.E-09	–
73	hsa-miR-1229-5p	6.30.E-09	+
74	hsa-miR-6820-5p	6.66.E-09	–
75	hsa-miR-6777-5p	7.32.E-09	–
76	hsa-miR-3917	7.71.E-09	–
77	hsa-miR-5787	7.78.E-09	+
78	hsa-miR-4286	1.22.E-08	–
79	hsa-miR-6877-5p	1.34.E-08	–
80	hsa-miR-1225-3p	1.56.E-08	+
81	hsa-miR-6088	1.57.E-08	–
82	hsa-miR-6800-5p	1.94.E-08	+
83	hsa-miR-1246	3.37.E-08	–
84	hsa-miR-4467	4.44.E-08	+
85	hsa-miR-4419b	5.34.E-08	–
86	hsa-miR-1914-3p	6.12.E-08	–
87	hsa-miR-4632-5p	7.12.E-08	+
88	hsa-miR-1915-5p	7.21.E-08	–
89	hsa-miR-3940-5p	7.68.E-08	+
90	hsa-miR-1185-2-3p	8.95.E-08	+
91	hsa-miR-6746-5p	1.20.E-07	–
92	hsa-miR-5001-5p	1.89.E-07	–
93	hsa-miR-1228-5p	2.11.E-07	+
94	hsa-miR-5572	2.20.E-07	+
95	hsa-miR-4327	2.34.E-07	+

TABLE 2-continued

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in liver cancer patient relative to healthy subject
96	hsa-miR-4638-5p	2.46.E−07	−
97	hsa-miR-6799-5p	3.24.E−07	+
98	hsa-miR-6861-5p	5.31.E−07	−
99	hsa-miR-6727-5p	5.46.E−07	−
100	hsa-miR-4513	7.37.E−07	−
101	hsa-miR-6805-3p	1.20.E−06	+
102	hsa-miR-6808-5p	1.48.E−06	+
103	hsa-miR-4449	1.92.E−06	+
104	hsa-miR-1199-5p	1.96.E−06	−
105	hsa-miR-1275	2.60.E−06	+
106	hsa-miR-4792	3.93.E−06	+
107	hsa-miR-4443	4.56.E−06	+
108	hsa-miR-6891-5p	4.68.E−06	+
109	hsa-miR-6826-5p	5.09.E−06	−
110	hsa-miR-6807-5p	5.61.E−06	+
111	hsa-miR-7150	5.87.E−06	+
112	hsa-miR-4534	6.23.E−06	+
113	hsa-miR-4476	6.58.E−06	−
114	hsa-miR-4649-5p	6.78.E−06	−
115	hsa-miR-4525	6.95.E−06	−
116	hsa-miR-1915-3p	7.86.E−06	+
117	hsa-miR-4516	9.89.E−06	−
118	hsa-miR-4417	1.02.E−05	+
119	hsa-miR-642b-3p	1.44.E−05	−
120	hsa-miR-3141	1.52.E−05	+
121	hsa-miR-5100	1.70.E−05	−
122	hsa-miR-6848-5p	2.10.E−05	+
123	hsa-miR-4739	2.86.E−05	+
124	hsa-miR-4459	3.57.E−05	+
125	hsa-miR-1237-5p	3.74.E−05	+
126	hsa-miR-296-3p	4.27.E−05	−
127	hsa-miR-4665-3p	4.37.E−05	+
128	hsa-miR-6786-5p	6.36.E−05	+
129	hsa-miR-4258	7.87.E−05	−
130	hsa-miR-6510-5p	8.68.E−05	+
131	hsa-miR-1343-5p	8.90.E−05	+
132	hsa-miR-1247-3p	1.33.E−04	+
133	hsa-miR-6805-5p	1.34.E−04	+
134	hsa-miR-4492	1.62.E−04	+
135	hsa-miR-1469	1.93.E−04	+
136	hsa-miR-1268b	2.29.E−04	+
137	hsa-miR-6858-5p	2.37.E−04	+
138	hsa-miR-3937	3.14.E−04	+
139	hsa-miR-939-5p	3.53.E−04	+
140	hsa-miR-3656	3.91.E−04	+
141	hsa-miR-744-5p	4.32.E−04	+
142	hsa-miR-4687-3p	4.42.E−04	+
143	hsa-miR-4763-3p	4.53.E−04	+
144	hsa-miR-3620-5p	5.43.E−04	+
145	hsa-miR-3195	6.21.E−04	+
146	hsa-miR-6842-5p	6.44.E−04	+
147	hsa-miR-4707-5p	7.50.E−04	+
148	hsa-miR-642a-3p	8.01.E−04	+
149	hsa-miR-7113-3p	8.81.E−04	+
150	hsa-miR-4728-5p	1.13.E−03	−
151	hsa-miR-5195-3p	1.39.E−03	−
152	hsa-miR-1185-1-3p	1.99.E−03	+
153	hsa-miR-6774-5p	2.01.E−03	+
154	hsa-miR-8059	2.34.E−03	−
155	hsa-miR-3131	2.51.E−03	−
156	hsa-miR-7847-3p	2.78.E−03	−
157	hsa-miR-4463	3.86.E−03	+
158	hsa-miR-128-2-5p	4.01.E−03	−
159	hsa-miR-4508	4.42.E−03	+
160	hsa-miR-6806-5p	4.85.E−03	−
161	hsa-miR-7111-5p	5.18.E−03	+
162	hsa-miR-6782-5p	5.20.E−03	+
163	hsa-miR-4734	6.28.E−03	+
164	hsa-miR-3162-5p	8.46.E−03	+
165	hsa-miR-887-3p	8.47.E−03	+
166	hsa-miR-6752-5p	8.98.E−03	+
167	hsa-miR-6724-5p	9.90.E−03	+
168	hsa-miR-23b-3p	4.55.E−23	−
169	hsa-miR-23a-3p	4.37.E−21	−
170	hsa-miR-625-3p	8.87.E−20	+
171	hsa-miR-1228-3p	1.35.E−19	+
172	hsa-miR-614	2.37.E−18	−
173	hsa-miR-1913	5.84.E−18	+
174	hsa-miR-92a-2-5p	9.35.E−16	+
175	hsa-miR-187-5p	1.18.E−15	−
176	hsa-miR-16-5p	2.32.E−14	−
177	hsa-miR-92b-3p	2.82.E−12	−
178	hsa-miR-150-3p	8.73.E−11	−
179	hsa-miR-564	1.08.E−09	−
180	hsa-miR-125a-3p	1.64.E−07	−
181	hsa-miR-92b-5p	5.34.E−07	+
182	hsa-miR-92a-3p	6.00.E−06	−
183	hsa-miR-663a	7.49.E−04	+

TABLE 3

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1	95.5	97.1	95	97	93.8	98
2	97	97.1	97	95.5	93.8	96
3	91.8	82.4	95	90.9	93.8	90
4	96.3	91.2	98	95.5	87.5	98
5	96.3	88.2	99	92.4	75	98
6	94.8	88.2	97	95.5	87.5	98
7	92.5	73.5	99	90.9	62.5	100
8	94.8	88.2	97	92.4	81.2	96
9	91.8	82.4	95	95.5	93.8	96
10	94.7	94.1	94.9	92.4	93.8	92
11	94	91.2	95	86.4	75	90
12	91.8	76.5	97	93.9	93.8	94
13	91.8	70.6	99	89.4	62.5	98
14	97	91.2	99	97	93.8	98
15	91.8	73.5	98	87.9	56.2	98
16	90.3	64.7	99	87.9	56.2	98
17	90.3	67.6	98	81.8	56.2	90
18	88.1	58.8	98	84.8	43.8	98

TABLE 3-continued

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
19	88.1	76.5	92	90.9	93.8	90
20	92.5	73.5	99	86.4	50	98
21	92.5	79.4	97	92.4	68.8	100
22	88.8	58.8	99	97	87.5	100
23	91	73.5	97	90.9	93.8	90
24	91.8	79.4	96	84.8	81.2	86
25	89.6	82.4	92	93.9	87.5	96
26	88.8	76.5	93	84.8	50	96
27	91.8	73.5	98	89.4	62.5	98
28	83.6	50	95	86.4	56.2	96
29	88.8	73.5	94	87.9	68.8	94
30	85.8	64.7	93	86.4	81.2	88
31	88.8	76.5	93	83.3	81.2	84
32	89.6	61.8	99	89.4	62.5	98
33	89.6	79.4	93	92.4	87.5	94
34	86.6	64.7	94	84.8	68.8	90
35	88.1	64.7	96	87.9	75	92
36	86.6	50	99	80.3	31.2	96
37	84.3	64.7	91	89.4	75	94
38	85.8	50	98	86.4	43.8	100
39	87.3	52.9	99	92.4	75	98
40	85.1	64.7	92	78.8	62.5	84
41	94	85.3	97	93.9	93.8	94
42	85.8	52.9	97	84.8	50	96
43	82.1	64.7	88	86.4	75	90
44	82.1	50	93	80.3	56.2	88
45	88.1	70.6	94	84.8	62.5	92
46	82.8	52.9	93	86.4	62.5	94
47	86.6	55.9	97	89.4	68.8	96
48	88.1	67.6	95	92.4	87.5	94
49	82.8	50	94	72.7	25	88
50	94	85.3	97	89.4	75	94
51	84.3	55.9	94	83.3	62.5	90
52	83.6	41.2	98	86.4	43.8	100
53	85.8	52.9	97	84.8	43.8	98
54	91	79.4	95	87.9	75	92
55	86.6	58.8	96	90.9	68.8	98
56	83.6	55.9	93	84.8	62.5	92
57	86.6	67.6	93	89.4	68.8	96
58	85.1	55.9	95	92.4	68.8	100
59	85.1	47.1	98	81.8	31.2	98
60	82.1	50	93	89.4	68.8	96
61	86.6	67.6	93	86.4	62.5	94
62	85.8	61.8	94	87.9	62.5	96
63	82.1	58.8	90	84.8	75	88
64	83.6	61.8	91	89.4	62.5	98
65	85.1	64.7	92	89.4	75	94
66	85.8	52.9	97	78.8	31.2	94
67	84.3	58.8	93	83.3	50	94
68	84.3	47.1	97	90.9	68.8	98
69	80.6	26.5	99	80.3	18.8	100
70	86.6	55.9	97	83.3	50	94
71	83.6	38.2	99	84.8	37.5	100
72	79.1	41.2	92	74.2	31.2	88
73	85.1	55.9	95	86.4	56.2	96
74	85.8	47.1	99	81.8	31.2	98
75	82.1	32.4	99	83.3	31.2	100
76	82.1	32.4	99	81.8	37.5	96
77	81.3	32.4	98	87.9	50	100
78	82.1	38.2	97	78.8	25	96
79	79.1	41.2	92	78.8	37.5	92
80	88.8	64.7	97	95.5	81.2	100
81	79.1	47.1	90	80.3	43.8	92
82	84.3	52.9	95	81.8	50	92
83	82.1	41.2	96	78.8	31.2	94
84	76.1	41.2	88	84.8	50	96
85	79.9	32.4	96	78.8	18.8	98
86	83.6	55.9	93	83.3	68.8	88
87	86.6	50	99	80.3	18.8	100
88	82.1	41.2	96	86.4	56.2	96
89	82.1	38.2	97	80.3	37.5	94
90	83.6	50	95	80.3	43.8	92
91	78.4	44.1	90	84.8	62.5	92
92	88.1	64.7	96	81.8	37.5	96
93	82.8	50	94	84.8	56.2	94

TABLE 3-continued

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
94	88.1	67.6	95	84.8	56.2	94
95	82.8	50	94	77.3	31.2	92
96	82.1	35.3	98	80.3	18.8	100
97	84.3	50	96	77.3	18.8	96
98	79.1	41.2	92	78.8	37.5	92
99	83.6	55.9	93	90.9	68.8	98
100	76.1	14.7	97	81.8	31.2	98
101	78.4	44.1	90	78.8	31.2	94
102	79.9	32.4	96	77.3	31.2	92
103	81.3	41.2	95	75.8	12.5	96
104	82.1	44.1	95	84.8	50	96
105	77.6	32.4	93	77.3	25	94
106	84.3	50	96	86.4	50	98
107	85.1	50	97	86.4	50	98
108	82.1	47.1	94	87.9	50	100
109	79.9	26.5	98	77.3	6.2	100
110	79.1	35.3	94	78.8	31.2	94
111	84.3	44.1	98	83.3	31.2	100
112	80.6	35.3	96	75.8	12.5	96
113	78.4	20.6	98	81.8	25	100
114	83.6	47.1	96	86.4	56.2	96
115	79.1	38.2	93	80.3	25	98
116	82.1	44.1	95	78.8	31.2	94
117	84.3	50	96	87.9	62.5	96
118	82.8	41.2	97	83.3	43.8	96
119	82.8	41.2	97	83.3	31.2	100
120	79.1	23.5	98	75.8	18.8	94
121	82	39.4	96	74.2	12.5	94
122	77.6	32.4	93	74.2	31.2	88
123	82.1	38.2	97	80.3	31.2	96
124	80.6	32.4	97	83.3	37.5	98
125	76.9	20.6	96	78.8	18.8	98
126	77.6	20.6	97	78.8	25	96
127	82.8	35.3	99	83.3	37.5	98
128	79.9	32.4	96	71.2	37.5	82
129	82.8	38.2	98	81.8	31.2	98
130	82.1	32.4	99	83.3	31.2	100
131	83.6	44.1	97	83.3	37.5	98
132	85.8	44.1	100	84.8	43.8	98
133	78.4	26.5	96	81.8	43.8	94
134	79.9	35.3	95	77.3	31.2	92
135	78.4	14.7	100	72.7	0	96
136	69.4	8.8	90	68.2	6.2	88
137	77.6	14.7	99	72.7	0	96
138	77.6	29.4	94	78.8	25	96
139	82.1	32.4	99	80.3	31.2	96
140	75.4	20.6	94	77.3	12.5	98
141	76.9	20.6	96	83.3	31.2	100
142	74.6	20.6	93	81.8	31.2	98
143	77.6	23.5	96	80.3	25	98
144	78.4	29.4	95	77.3	31.2	92
145	76.9	23.5	95	74.2	12.5	94
146	81.3	29.4	99	86.4	50	98
147	73.1	8.8	95	72.7	0	96
148	79.9	26.5	98	77.3	12.5	98
149	78.4	17.6	99	75.8	12.5	96
150	74.6	23.5	92	74.2	18.8	92
151	73.9	8.8	96	75.8	6.2	98
152	79.9	29.4	97	74.2	12.5	94
153	73.9	11.8	95	72.7	0	96
154	75.4	14.7	96	75.8	12.5	96
155	79.1	23.5	98	77.3	12.5	98
156	75.4	5.9	99	77.3	6.2	100
157	76.1	20.6	95	77.3	18.8	96
158	80.6	29.4	98	78.8	12.5	100
159	73.9	11.8	95	75.8	31.2	90
160	76.1	5.9	100	75.8	0	100
161	79.1	23.5	98	78.8	12.5	100
162	79.1	17.6	100	77.3	18.8	96
163	72.4	8.8	94	78.8	31.2	94
164	75.4	14.7	96	72.7	6.2	94
165	70.9	2.9	94	68.2	0	90
166	76.1	14.7	97	72.7	6.2	94
167	76.9	23.5	95	74.2	12.5	94
168	88.8	64.7	97	81.8	43.8	94

TABLE 3-continued

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
169	87.3	58.8	97	80.3	37.5	94
170	91	76.5	96	90.9	87.5	92
171	91.8	85.3	94	89.4	87.5	90
172	87.3	79.4	90	89.4	75	94
173	88.8	79.4	92	87.7	68.8	93.9
174	89.6	76.5	94	84.8	62.5	92
175	90.3	70.6	97	93.9	81.2	98
176	85.8	55.9	96	83.3	43.8	96
177	86.6	52.9	98	83.3	37.5	98
178	83.6	38.2	99	81.8	50	92
179	82.8	41.2	97	84.8	43.8	98
180	84.3	41.2	99	87.9	50	100
181	82.1	32.4	99	75.8	0	100
182	82.1	32.4	99	78.8	18.8	98
183	76.9	14.7	98	77.3	6.2	100

TABLE 4

SEQ ID NO:	Discriminant coefficient	Constant term
1	2.471	17.511
2	3.389	32.503
3	4.221	29.467
4	5.669	61.422
5	2.340	14.902
6	3.403	21.347
7	1.666	16.714
8	3.780	23.286
9	1.162	7.705
10	3.871	23.895
11	3.327	20.777
12	3.912	32.887
13	1.850	20.690
14	2.777	21.161
15	1.469	12.157
16	1.640	15.602
17	1.594	20.057
18	1.741	16.417
19	1.740	14.012
20	2.167	12.838
21	3.215	24.454
22	2.867	24.605
23	3.272	30.031
24	5.400	67.222
25	4.398	44.949
26	4.110	47.240
27	8.336	105.482
28	6.984	90.484
29	3.912	29.950
30	4.452	41.269
31	3.737	30.649
32	1.541	12.525
33	1.731	9.319
34	6.775	65.355
35	4.246	28.999
36	0.707	5.520
37	2.475	20.255
38	1.782	9.870
39	1.749	10.960
40	2.724	20.676
41	1.635	11.008
42	2.017	16.782
43	3.750	27.935
44	3.268	30.852
45	3.074	20.807
46	4.135	48.094
47	2.722	23.696
48	4.645	49.638
49	4.364	34.762
50	2.395	13.357
51	5.700	60.009

TABLE 4-continued

SEQ ID NO:	Discriminant coefficient	Constant term
52	1.785	12.550
53	3.691	44.502
54	3.410	43.229
55	4.359	43.584
56	3.783	25.006
57	2.734	18.058
58	2.978	26.851
59	6.061	51.915
60	2.729	18.883
61	2.150	17.585
62	5.256	63.263
63	3.936	30.117
64	4.508	41.792
65	2.386	16.961
66	1.810	12.154
67	2.969	28.301
68	3.512	34.056
69	1.951	12.101
70	3.135	22.180
71	1.606	9.267
72	2.696	34.139
73	4.474	34.903
74	2.012	14.274
75	1.959	12.395
76	2.215	12.602
77	5.057	66.741
78	1.620	11.678
79	4.288	30.633
80	2.430	13.696
81	3.351	33.938
82	3.921	34.024
83	1.278	9.389
84	2.183	21.651
85	1.944	11.599
86	4.824	36.279
87	3.858	31.074
88	1.277	7.779
89	4.555	56.233
90	1.520	8.345
91	3.667	23.791
92	3.455	26.548
93	3.821	45.609
94	1.784	12.053
95	4.842	42.664
96	1.392	8.122
97	3.251	27.595
98	4.026	29.199
99	5.471	69.803
100	2.281	13.200
101	2.499	18.849
102	5.118	35.429

TABLE 4-continued

SEQ ID NO:	Discriminant coefficient	Constant term
103	3.691	24.076
104	2.471	16.246
105	2.973	21.963
106	1.588	10.669
107	2.017	13.094
108	4.206	32.002
109	1.659	9.895
110	2.739	16.192
111	3.174	24.976
112	2.780	19.682
113	1.225	8.488
114	2.404	24.762
115	2.895	19.963
116	4.205	46.806
117	4.490	59.177
118	5.016	41.382
119	2.142	20.182
120	4.030	28.787
121	2.093	21.502
122	4.832	36.040
123	3.672	42.382
124	3.305	27.456
125	4.919	62.904
126	1.924	11.325
127	2.696	15.869
128	7.275	92.098
129	1.903	17.010
130	1.935	12.644
131	3.379	35.351
132	2.384	15.077
133	6.549	74.981
134	5.238	55.302
135	2.785	28.718
136	3.118	31.040
137	3.097	23.331
138	4.424	38.383
139	1.611	12.320
140	4.840	56.003
141	2.484	17.251
142	3.851	37.749
143	3.720	31.374
144	3.991	31.836
145	4.065	33.772
146	2.441	14.617
147	3.795	27.973
148	2.362	18.895
149	2.354	13.716
150	5.065	35.714
151	2.922	20.137
152	1.539	9.313
153	4.631	31.436
154	3.326	25.477
155	2.223	15.649
156	2.416	15.308
157	4.655	51.632
158	2.552	27.736
159	6.563	85.503
160	2.281	14.772
161	5.241	39.899
162	2.291	14.195
163	6.256	74.602
164	2.920	22.423
165	2.285	16.474
166	3.720	42.108
167	4.806	47.920
168	1.156	5.990
169	1.212	6.218
170	3.292	19.092
171	4.244	27.332
172	1.867	12.024
173	3.494	22.197
174	2.062	19.948
175	1.942	18.936
176	0.886	4.794
177	1.182	6.543
178	1.678	10.850
179	1.358	7.646
180	1.032	6.311
181	2.498	20.322
182	1.203	7.922
183	2.779	28.552

TABLE 5-1

Training cohort

Sample name	Cancer stage	AFP (ng/mL)	CEA (ng/mL)	CA19-9 (U/mL)	PIVKA-II (mAU/mL)
HC03	I	13.2	3.1	—	99
HC04	I	37210	1	—	13550
HC05	IV	3	—	—	18
HC06	I	26.1	5.7	—	136
HC07	III	3.2	3.4	—	2452
HC09	II	34.7	5	26.2	1932
HC10	I	74	2.6	—	10
HC12	I	3.4	—	—	39
HC13	III	—	0.6	5.1	—
HC15	II	—	1.9	0.1	—
HC17	II	2.3	—	—	556
HC18	IV	36145	—	—	167
HC19	I	8.5	3.7	—	13
HC20	I	4.6	3.2	6.4	344
HC23	III	151.3	1.9	—	29521
HC24	III	103299	1.9	—	55837
HC25	I	179.7	12.1	—	220
HC26	I	25.3	1.4	—	36
HC27	I	8.5	4.7	—	28
HC29	I	29.2	—	—	979
HC30	IIIB	77.4	—	—	176940
HC31	II	7	—	—	34
HC32	III	2.2	1.8	—	40
HC34	II	6.9	—	—	688
HC36	II	25.3	1.9	—	3481
HC38	I	5.4	4.8	—	92
HC40	IIIB	5.7	—	—	95
HC41	II	93.7	5.8	104.9	26
HC42	I	1.9	6.5	—	25
HC45	II	10.3	—	—	51
HC47	IIIC	235.5	—	—	3601
HC48	I	107.9	—	—	52
HC49	I	4.5	4.3	26.7	22
HC50	II	133338	2.9	—	829
	Sensitivity	56.3%	18.2%	16.7%	65.6%

TABLE 5-2

Validation cohort

Sample name	Cancer stage	AFP (ng/mL)	CEA (ng/mL)	CA19-9 (U/mL)	PIVKA-II (mAU/mL)
HC01	II	10.8	2.8	—	678
HC02	I	3.8	1.4	11.4	26
HC08	I	13	3	—	245
HC11	I	17.2	3.4	—	15
HC14	I	1.8	5.7	—	18
HC16	I	6		—	21
HC21	II	5.3	5.3	14.8	22
HC22	I	1.7	—	—	76
HC28	I	—	4.4	11	—
HC33	III	40	1.1	—	25
HC35	II	4.2	5.2	—	20
HC37	III	59992	—	—	14358
HC39	II	555	—	—	194
HC43	I	18	—	—	32
HC44	I	7.5	1	32.7	462
HC46	I	1075	—	—	46
	Sensitivity	53.3%	30.0%	0.0%	46.7%

The reference values of AFP, CEA, CA19-9, and PIVKA-II were 10 ng/mL, 5 ng/mL, 37 U/mL, and 40 mAU/mL, respectively. Each sample that exhibited a measurement value equal to or higher than the reference values was determined to be positive, and the sensitivity of each tumor marker was calculated.

TABLE 6

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_2	99.3	100	99	100	100	100
1_3	100	100	100	98.5	100	98
1_4	99.3	100	99	100	100	100
1_5	97.8	97.1	98	97	93.8	98
1_6	99.3	97.1	100	97	93.8	98
1_7	96.3	91.2	98	97	87.5	100
1_8	100	100	100	97	93.8	98
1_9	97.8	97.1	98	97	100	96
1_10	99.2	100	99	100	100	100
1_11	98.5	100	98	97	93.8	98
1_12	97.8	100	97	97	93.8	98
1_13	98.5	97.1	99	98.5	93.8	100
1_14	99.3	100	99	98.5	93.8	100
1_15	97.8	94.1	99	98.5	93.8	100
1_16	97.8	94.1	99	97	93.8	98
1_17	99.3	100	99	97	100	96
1_18	97.8	97.1	98	97	93.8	98
1_19	96.3	94.1	97	97	93.8	98
1_20	96.3	94.1	97	97	93.8	98
1_21	95.5	94.1	96	97	93.8	98
1_22	97	94.1	98	97	93.8	98
1_23	97.8	97.1	98	98.5	100	98
1_24	98.5	100	98	97	93.8	98
1_25	97.8	97.1	98	97	93.8	98
1_26	97	97.1	97	97	93.8	98
1_27	97.8	97.1	98	95.5	93.8	96
1_28	97.8	100	97	97	93.8	98
1_29	97.8	100	97	97	100	96
1_30	98.5	97.1	99	93.9	87.5	96
1_31	95.5	91.2	97	97	93.8	98
1_32	99.3	100	99	97	100	96
1_33	96.3	94.1	97	97	93.8	98
1_34	96.3	97.1	96	97	93.8	98
1_35	97.8	97.1	98	97	93.8	98
1_36	99.3	100	99	98.5	93.8	100
1_37	97	94.1	98	97	93.8	98
1_38	98.5	97.1	99	97	93.8	98
1_39	99.3	97.1	100	100	100	100
1_40	97	97.1	97	97	93.8	98
1_41	95.5	94.1	96	97	93.8	98
1_42	96.3	97.1	96	97	93.8	98
1_43	96.3	94.1	97	97	93.8	98
1_44	98.5	100	98	97	100	96
1_45	97.8	97.1	98	97	93.8	98
1_46	97	97.1	97	97	93.8	98
1_47	97	94.1	98	97	93.8	98
1_48	97.8	97.1	98	97	93.8	98
1_49	98.5	97.1	99	98.5	93.8	100
1_50	96.3	97.1	96	97	93.8	98
1_51	97	97.1	97	97	93.8	98
1_52	99.3	100	99	98.5	100	98
1_53	95.5	97.1	95	97	93.8	98
1_54	96.3	94.1	97	97	93.8	98
1_55	97.8	97.1	98	97	93.8	98
1_56	96.3	97.1	96	97	93.8	98
1_57	97	94.1	98	97	93.8	98
1_58	96.3	94.1	97	97	93.8	98
1_59	97	94.1	98	98.5	93.8	100
1_60	97	97.1	97	97	93.8	98
1_61	95.5	94.1	96	97	93.8	98
1_62	97	94.1	98	97	93.8	98
1_63	96.3	94.1	97	97	93.8	98
1_64	97.8	94.1	99	97	93.8	98
1_65	97.8	97.1	98	97	93.8	98
1_66	97.8	97.1	98	97	93.8	98
1_67	97	94.1	98	97	93.8	98
1_68	98.5	100	98	98.5	100	98
1_69	96.3	94.1	97	97	93.8	98
1_70	97.8	94.1	99	97	93.8	98
1_71	97.8	97.1	98	97	93.8	98

TABLE 6-continued

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1__72	97.8	100	97	95.5	100	94
1__73	95.5	94.1	96	97	93.8	98
1__74	99.3	100	99	98.5	100	98
1__75	98.5	100	98	97	93.8	98
1__76	96.3	97.1	96	97	93.8	98
1__77	97.8	97.1	98	97	93.8	98
1__78	97	97.1	97	97	93.8	98
1__79	97	97.1	97	97	93.8	98
1__80	97	94.1	98	95.5	87.5	98
1__81	98.5	97.1	99	95.5	93.8	96
1__82	95.5	97.1	95	97	93.8	98
1__83	96.3	91.2	98	97	93.8	98
1__84	97.8	97.1	98	97	93.8	98
1__85	96.3	97.1	96	97	93.8	98
1__86	97	97.1	97	95.5	93.8	96
1__87	97	97.1	97	97	93.8	98
1__88	96.3	94.1	97	98.5	100	98
1__89	95.5	97.1	95	95.5	93.8	96
1__90	98.5	100	98	95.5	93.8	96
1__91	96.3	97.1	96	97	93.8	98
1__92	97	97.1	97	97	93.8	98
1__93	97	100	96	95.5	93.8	96
1__94	96.3	94.1	97	97	93.8	98
1__95	97	97.1	97	97	93.8	98
1__96	99.3	100	99	97	100	96
1__97	97	100	96	95.5	93.8	96
1__98	97	100	96	95.5	93.8	96
1__99	97	97.1	97	97	93.8	98
1__100	98.5	100	98	95.5	93.8	96
1__101	97.8	100	97	93.9	93.8	94
1__102	97.8	100	97	97	93.8	98
1__103	97	97.1	97	97	93.8	98
1__104	97.8	97.1	98	97	93.8	98
1__105	96.3	97.1	96	97	93.8	98
1__106	97	100	96	95.5	93.8	96
1__107	96.3	97.1	96	97	93.8	98
1__108	96.3	97.1	96	95.5	93.8	96
1__109	96.3	97.1	96	97	93.8	98
1__110	97	97.1	97	98.5	100	98
1__111	97.8	100	97	97	100	96
1__112	96.3	97.1	96	97	93.8	98
1__113	98.5	100	98	97	100	96
1__114	96.3	100	95	95.5	93.8	96
1__115	97.8	97.1	98	98.5	100	98
1__116	95.5	97.1	95	97	93.8	98
1__117	97	94.1	98	97	93.8	98
1__118	95.5	97.1	95	97	93.8	98
1__119	97	97.1	97	97	93.8	98
1__120	95.5	97.1	95	97	93.8	98
1__121	97	97	97	97	93.8	98
1__122	95.5	97.1	95	97	93.8	98
1__123	97	97.1	97	98.5	100	98
1__124	95.5	97.1	95	97	93.8	98
1__125	98.5	97.1	99	97	93.8	98
1__126	96.3	94.1	97	93.9	93.8	94
1__127	97	97.1	97	98.5	100	98
1__128	96.3	97.1	96	95.5	93.8	96
1__129	97	100	96	97	100	96
1__130	95.5	97.1	95	97	93.8	98
1__131	97	100	96	93.9	93.8	94
1__132	96.3	94.1	97	97	93.8	98
1__133	96.3	97.1	96	95.5	93.8	96
1__134	98.5	100	98	97	93.8	98
1__135	98.5	97.1	99	95.5	93.8	96
1__136	97	97.1	97	97	93.8	98
1__137	97	97.1	97	98.5	100	98
1__138	96.3	97.1	96	97	93.8	98
1__139	96.3	94.1	97	97	93.8	98
1__140	96.3	97.1	96	97	93.8	98
1__141	97.8	97.1	98	97	100	96
1__142	95.5	94.1	96	97	93.8	98
1__143	95.5	97.1	95	97	93.8	98
1__144	95.5	97.1	95	97	93.8	98
1__145	97	94.1	98	97	93.8	98
1__146	95.5	94.1	96	97	93.8	98

TABLE 6-continued

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1_147	98.5	97.1	99	97	93.8	98
1_148	96.3	94.1	97	97	93.8	98
1_149	95.5	97.1	95	97	93.8	98
1_150	95.5	97.1	95	97	93.8	98
1_151	97.8	97.1	98	95.5	93.8	96
1_152	96.3	97.1	96	97	93.8	98
1_153	97.8	100	97	97	93.8	98
1_154	97.8	97.1	98	95.5	93.8	96
1_155	98.5	97.1	99	97	93.8	98
1_156	96.3	97.1	96	97	93.8	98
1_157	97	97.1	97	95.5	93.8	96
1_158	96.3	100	95	97	100	96
1_159	95.5	97.1	95	97	93.8	98
1_160	97	97.1	97	97	93.8	98
1_161	96.3	94.1	97	97	93.8	98
1_162	96.3	97.1	96	97	93.8	98
1_163	95.5	97.1	95	97	100	96
1_164	95.5	97.1	95	97	93.8	98
1_165	96.3	94.1	97	97	93.8	98
1_166	97	97.1	97	97	93.8	98
1_167	96.3	97.1	96	97	93.8	98
1_168	97	94.1	98	98.5	93.8	100
1_169	98.5	97.1	99	97	93.8	98
1_170	100	100	100	97	93.8	98
1_171	99.3	100	99	98.5	100	98
1_172	96.3	97.1	96	97	93.8	98
1_173	98.5	100	98	98.5	100	98
1_174	95.5	94.1	96	97	93.8	98
1_175	97	97.1	97	97	93.8	98
1_176	98.5	100	98	98.5	93.8	100
1_177	97.8	97.1	98	97	93.8	98
1_178	99.3	100	99	97	100	96
1_179	98.5	100	98	98.5	100	98
1_180	99.3	100	99	97	100	96
1_181	97.8	97.1	98	97	93.8	98
1_182	97	97.1	97	97	93.8	98
1_183	99.3	100	99	100	100	100

Example 3

Selection of Gene Marker Using all Samples and Method for Evaluating Liver Cancer Discriminant Performance of Acquired Gene Marker

In this Example, the samples in the training cohort and the validation cohort used in Examples 1 and 2 were integrated, and selection of a gene marker and evaluation of its liver cancer discriminant performance were conducted using all of the samples.

Specifically, the miRNA expression levels in the serum of the 50 liver cancer patients and the 150 healthy subjects obtained in the above-mentioned Reference Examples were normalized by quantile normalization. In order to acquire diagnostic markers with higher reliability, only genes having a gene expression level of 2^6 or higher in 50% or more of the samples in either of the liver cancer patient group or the healthy subject group were selected in the gene marker selection. In order to further acquire statistical significance for discriminating a liver cancer patient group from a healthy subject group, the P value obtained by two-tailed t-test assuming equal variance as to each gene expression level was corrected by the Bonferroni method, and genes that satisfied $p<0.01$ were selected as gene markers for use in explanatory variables of a discriminant. The acquired genes are described in Table 7. In this way, hsa-miR-4688, hsa-miR-4648, hsa-miR-6085, hsa-miR-6126, hsa-miR-6880-5p, hsa-miR-328-5p, hsa-miR-6768-5p, hsa-miR-3180, hsa-miR-6087, hsa-miR-1273g-3p, hsa-miR-1225-5p, hsa-miR-3196, hsa-miR-4695-5p, hsa-miR-6732-5p, hsa-miR-638, hsa-miR-6813-5p, hsa-miR-665, hsa-miR-486-3p, hsa-miR-4466, hsa-miR-30c-1-3p, hsa-miR-3621, hsa-miR-6743-5p, hsa-miR-4298, hsa-miR-4741, hsa-miR-3619-3p, hsa-miR-6824-5p, hsa-miR-5698, hsa-miR-371a-5p, hsa-miR-4488, hsa-miR-1233-5p, hsa-miR-4723-5p, hsa-miR-24-3p, hsa-miR-1238-5p, hsa-miR-4442, hsa-miR-3928-3p, hsa-miR-6716-5p, hsa-miR-6089, hsa-miR-6124, hsa-miR-6778-5p, hsa-miR-557 and hsa-miR-6090 genes represented by SEQ ID NOs: 184 to 224 were found as liver cancer markers relative to the healthy subjects, in addition to the genes described in Table 2. As with the polynucleotides shown in SEQ ID NOs: 1 to 183, the results obtained about the polynucleotides shown in SEQ ID NOs: 184 to 224 also showed that the expression level measurement values were significantly lower (−) or higher (+) in the liver cancer patient group than in the healthy subject group (Table 7). These results were able to be validated in the validation cohort. Thus, the presence or absence of liver cancer in the newly obtained samples can be determined by the methods described in Examples 1 and 2 by using the gene expression level measurement values described in Table 7 either alone or in combination with the gene expression level measurement values described in Table 2.

TABLE 7

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in liver cancer patient relative to healthy subject
1	hsa-miR-1343-3p	7.76.E−56	−
2	hsa-miR-6726-5p	1.12.E−51	−
3	hsa-miR-6515-3p	4.93.E−36	+
4	hsa-miR-4651	9.12.E−42	−
5	hsa-miR-4257	2.81.E−42	−
6	hsa-miR-3188	1.06.E−41	+
7	hsa-miR-6131	1.97.E−37	−
8	hsa-miR-6766-3p	4.59.E−35	+
9	hsa-miR-7641	2.35.E−36	−
10	hsa-miR-1249	2.50.E−34	+
11	hsa-miR-3679-3p	5.67.E−31	+
12	hsa-miR-6787-5p	9.25.E−36	−
13	hsa-miR-4454	1.38.E−34	−
14	hsa-miR-3135b	3.23.E−23	−
15	hsa-miR-6765-3p	8.15.E−32	−
16	hsa-miR-7975	4.38.E−28	−
17	hsa-miR-204-3p	2.40.E−25	−
18	hsa-miR-7977	6.65.E−27	−
19	hsa-miR-7110-5p	2.91.E−28	+
20	hsa-miR-6717-5p	4.18.E−23	−
21	hsa-miR-6870-5p	2.08.E−27	+
22	hsa-miR-663b	1.18.E−29	−
23	hsa-miR-6875-5p	1.80.E−24	+
24	hsa-miR-8072	1.13.E−21	+
25	hsa-miR-6816-5p	9.86.E−26	+
26	hsa-miR-4281	1.18.E−24	−
27	hsa-miR-6729-5p	1.39.E−22	+
28	hsa-miR-8069	9.35.E−19	+
29	hsa-miR-4706	1.28.E−23	−
30	hsa-miR-7108-5p	3.30.E−21	+
31	hsa-miR-4433b-3p	1.04.E−21	+
32	hsa-miR-6893-5p	7.87.E−23	−
33	hsa-miR-6857-5p	1.05.E−22	+
34	hsa-miR-1227-5p	5.00.E−23	+
35	hsa-miR-6741-5p	2.98.E−21	−
36	hsa-miR-451a	1.60.E−19	−
37	hsa-miR-8063	1.20.E−22	−
38	hsa-miR-3622a-5p	8.16.E−21	−
39	hsa-miR-615-5p	1.17.E−21	−
40	hsa-miR-128-1-5p	8.49.E−17	+
41	hsa-miR-6825-5p	4.10.E−25	+
42	hsa-miR-1260b	4.23.E−20	−
43	hsa-miR-4433-3p	7.63.E−20	+
44	hsa-miR-4665-5p	1.92.E−15	−
45	hsa-miR-7845-5p	9.71.E−18	+
46	hsa-miR-1908-5p	6.59.E−21	+
47	hsa-miR-6840-3p	1.70.E−20	−
48	hsa-miR-6765-5p	3.32.E−19	+
49	hsa-miR-296-5p	5.14.E−14	+
50	hsa-miR-6781-5p	6.41.E−18	+
51	hsa-miR-423-5p	1.91.E−15	−
52	hsa-miR-3663-3p	1.67.E−16	−
53	hsa-miR-6784-5p	8.43.E−18	+
54	hsa-miR-6749-5p	2.59.E−20	−
55	hsa-miR-1231	1.33.E−14	+
56	hsa-miR-4746-3p	3.47.E−19	+
57	hsa-miR-6780b-5p	2.82.E−21	+
58	hsa-miR-4758-5p	4.87.E−15	−
59	hsa-miR-3679-5p	1.59.E−19	+
60	hsa-miR-3184-5p	6.75.E−18	+
61	hsa-miR-6125	8.43.E−17	+
62	hsa-miR-6721-5p	3.93.E−15	+
63	hsa-miR-6791-5p	1.78.E−17	+
64	hsa-miR-3185	5.38.E−17	+
65	hsa-miR-1260a	7.87.E−15	−
66	hsa-miR-3197	1.51.E−14	+
67	hsa-miR-6845-5p	2.09.E−16	+
68	hsa-miR-6887-5p	3.08.E−15	−
69	hsa-miR-6738-5p	1.83.E−16	−
70	hsa-miR-6872-3p	5.80.E−14	−
71	hsa-miR-4497	2.63.E−10	−
72	hsa-miR-1229-5p	1.21.E−14	+
73	hsa-miR-6820-5p	5.60.E−13	−
74	hsa-miR-6777-5p	7.03.E−15	−
75	hsa-miR-3917	7.63.E−13	−
76	hsa-miR-5787	5.42.E−15	+
77	hsa-miR-4286	1.57.E−12	−
78	hsa-miR-6877-5p	1.83.E−14	−
79	hsa-miR-1225-3p	4.77.E−11	+
80	hsa-miR-6088	4.12.E−13	−
81	hsa-miR-6800-5p	1.01.E−13	+
82	hsa-miR-1246	1.20.E−10	−
83	hsa-miR-4467	2.24.E−15	+
84	hsa-miR-4419b	3.03.E−12	−
85	hsa-miR-1914-3p	3.27.E−13	−
86	hsa-miR-4632-5p	6.04.E−12	+
87	hsa-miR-1915-5p	7.61.E−15	−
88	hsa-miR-3940-5p	7.23.E−12	+
89	hsa-miR-6746-5p	5.54.E−13	−
91	hsa-miR-5001-5p	2.14.E−13	−
92	hsa-miR-1228-5p	7.95.E−13	+
93	hsa-miR-5572	5.18.E−16	+
94	hsa-miR-4327	2.61.E−09	+
95	hsa-miR-4638-5p	1.48.E−10	−
96	hsa-miR-6799-5p	1.10.E−10	+
97	hsa-miR-6861-5p	8.44.E−11	−
98	hsa-miR-6727-5p	2.38.E−13	−
99	hsa-miR-4513	8.83.E−12	−
100	hsa-miR-6805-3p	1.08.E−12	+
101	hsa-miR-6808-5p	3.32.E−10	+
102	hsa-miR-4449	4.13.E−09	+
103	hsa-miR-1199-5p	1.45.E−11	−
104	hsa-miR-1275	2.47.E−08	+
105	hsa-miR-4792	9.54.E−13	+
106	hsa-miR-4443	4.44.E−10	+
107	hsa-miR-6891-5p	3.67.E−12	+
108	hsa-miR-6826-5p	5.10.E−11	−
109	hsa-miR-6807-5p	1.03.E−09	+
110	hsa-miR-7150	1.05.E−09	+
111	hsa-miR-4534	1.61.E−09	+
112	hsa-miR-4476	6.66.E−08	−
113	hsa-miR-4649-5p	1.12.E−10	−
114	hsa-miR-4525	4.68.E−12	−
115	hsa-miR-1915-3p	1.92.E−10	+
116	hsa-miR-4516	1.95.E−10	−
117	hsa-miR-4417	3.89.E−10	+
118	hsa-miR-642b-3p	3.82.E−10	−
119	hsa-miR-3141	1.02.E−08	+
120	hsa-miR-5100	4.74.E−08	−
121	hsa-miR-6848-5p	7.00.E−10	+
122	hsa-miR-4739	1.94.E−08	+
123	hsa-miR-4459	1.30.E−08	+
124	hsa-miR-1237-5p	1.04.E−08	+
125	hsa-miR-296-3p	9.28.E−08	−
126	hsa-miR-4665-3p	9.58.E−12	+
127	hsa-miR-6786-5p	7.26.E−06	+
128	hsa-miR-4258	4.38.E−08	−
129	hsa-miR-6510-5p	4.93.E−11	+
130	hsa-miR-1343-5p	1.77.E−10	+
131	hsa-miR-1247-3p	3.69.E−11	+
132	hsa-miR-6805-5p	1.78.E−09	+
133	hsa-miR-4492	1.28.E−07	+
134	hsa-miR-1469	8.04.E−06	+
135	hsa-miR-1268b	7.93.E−07	+
136	hsa-miR-6858-5p	2.19.E−06	+
137	hsa-miR-3937	5.07.E−06	+
138	hsa-miR-939-5p	3.71.E−10	+
139	hsa-miR-3656	9.45.E−10	+
140	hsa-miR-744-5p	6.81.E−08	+
141	hsa-miR-4687-3p	1.70.E−07	+
142	hsa-miR-4763-3p	1.79.E−06	+
143	hsa-miR-3620-5p	2.74.E−06	+
144	hsa-miR-3195	1.35.E−04	+
145	hsa-miR-6842-5p	9.98.E−12	+
146	hsa-miR-4707-5p	7.25.E−06	+
147	hsa-miR-642a-3p	1.31.E−06	+
148	hsa-miR-7113-3p	2.95.E−07	+
149	hsa-miR-4728-5p	3.51.E−06	−
150	hsa-miR-5195-3p	9.06.E−07	−
151	hsa-miR-1185-1-3p	3.35.E−05	+
152			

TABLE 7-continued

SEQ ID NO:	Gene name	P value after Bonferroni correction	Expression level in liver cancer patient relative to healthy subject
153	hsa-miR-6774-5p	5.14.E-04	+
154	hsa-miR-8059	1.37.E-05	-
155	hsa-miR-3131	6.97.E-08	-
156	hsa-miR-7847-3p	6.35.E-06	-
157	hsa-miR-4463	1.04.E-07	+
158	hsa-miR-128-2-5p	3.84.E-06	-
159	hsa-miR-4508	3.57.E-05	+
160	hsa-miR-6806-5p	2.04.E-06	-
161	hsa-miR-7111-5p	6.31.E-05	+
162	hsa-miR-6782-5p	2.11.E-07	+
163	hsa-miR-4734	1.79.E-05	+
164	hsa-miR-3162-5p	7.73.E-04	+
165	hsa-miR-887-3p	7.67.E-05	+
166	hsa-miR-6752-5p	7.74.E-05	+
167	hsa-miR-6724-5p	4.17.E-05	+
168	hsa-miR-23b-3p	1.17.E-30	-
169	hsa-miR-23a-3p	5.61.E-28	-
170	hsa-miR-625-3p	1.19.E-16	+
171	hsa-miR-1228-3p	7.80.E-28	+
172	hsa-miR-614	7.24.E-27	-
173	hsa-miR-1913	1.52.E-26	+
174	hsa-miR-92a-2-5p	5.94.E-24	+
175	hsa-miR-187-5p	1.72.E-26	-
176	hsa-miR-16-5p	4.14.E-20	-
177	hsa-miR-92b-3p	1.09.E-17	-
178	hsa-miR-150-3p	1.47.E-13	-
179	hsa-miR-564	2.36.E-15	-
180	hsa-miR-125a-3p	7.07.E-12	-
181	hsa-miR-92b-5p	8.01.E-10	+
182	hsa-miR-92a-3p	3.99.E-09	-
183	hsa-miR-663a	1.34.E-06	+
184	hsa-miR-4688	4.97.E-07	-
185	hsa-miR-4648	2.21.E-05	+
186	hsa-miR-6085	2.31.E-05	+
187	hsa-miR-6126	2.31.E-05	+
188	hsa-miR-6880-5p	2.44.E-05	+
189	hsa-miR-328-5p	2.90.E-05	+
190	hsa-miR-6768-5p	4.36.E-05	+
191	hsa-miR-3180	6.14.E-05	+
192	hsa-miR-6087	8.15.E-05	-
193	hsa-miR-1273g-3p	1.23.E-04	-
194	hsa-miR-1225-5p	1.23.E-04	+
195	hsa-miR-3196	1.32.E-04	+
196	hsa-miR-4695-5p	1.47.E-04	+
197	hsa-miR-6732-5p	2.45.E-04	+
198	hsa-miR-638	2.98.E-04	-
199	hsa-miR-6813-5p	3.27.E-04	+
200	hsa-miR-665	3.46.E-04	+
201	hsa-miR-486-3p	4.04.E-04	-
202	hsa-miR-4466	4.22.E-04	-
203	hsa-miR-30c-1-3p	5.71.E-04	+
204	hsa-miR-3621	8.32.E-04	-
205	hsa-miR-6743-5p	8.89.E-04	+
206	hsa-miR-4298	1.05.E-03	-
207	hsa-miR-4741	1.07.E-03	+
208	hsa-miR-3619-3p	1.11.E-03	+
209	hsa-miR-6824-5p	1.17.E-03	+
210	hsa-miR-5698	1.30.E-03	-
211	hsa-miR-371a-5p	1.51.E-03	-
212	hsa-miR-4488	1.85.E-03	-
213	hsa-miR-1233-5p	1.90.E-03	-
214	hsa-miR-4723-5p	2.05.E-03	+
215	hsa-miR-24-3p	2.09.E-03	-
216	hsa-miR-1238-5p	2.18.E-03	+
217	hsa-miR-4442	2.48.E-03	-
218	hsa-miR-3928-3p	2.71.E-03	+
219	hsa-miR-6716-5p	2.96.E-03	+
220	hsa-miR-6089	3.43.E-03	+
221	hsa-miR-6124	3.68.E-03	+
222	hsa-miR-6778-5p	4.10.E-03	-
223	hsa-miR-557	6.88.E-03	+
224	hsa-miR-6090	9.92.E-03	+

Example 4

Method for Evaluating Liver Cancer-Specific Discriminant Performance by Combination of Multiple Gene Markers Using Samples in the Validation Cohort

In this Example, novel additional gene markers for diagnosis were selected by comparing gene expression levels of miRNAs in sera of liver cancer patients with those of a control group consisting of healthy subjects, pancreatic cancer patients, bile duct cancer patients, stomach cancer patients, esophageal cancer patients, colorectal cancer patients, and benign pancreaticobiliary disease patients, in the same way as the method described in Example 1, and targeting the training cohort as the sample group described in Reference Example 2. One or two or more markers selected from the group consisting of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 714 to 729 thus selected and the gene markers selected in Example 1 were used to evaluate liver cancer-specific discriminant performance.

Specifically, first, the miRNA expression levels in the training cohort and the validation cohort obtained in Reference Example 2 mentioned above were combined and normalized by quantile normalization. Next, Fisher's discriminant analysis was conducted as to combinations of 1 to 4 expression level measurement values comprising at least one or more of the expression level measurement values of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 167 and 714 to 729, to construct a discriminant for determining the presence or absence of liver cancer. Next, accuracy, sensitivity, and specificity in the validation cohort were calculated using the discriminant thus prepared, with the liver cancer patient group as a positive sample group and, on the other hand, the healthy subject group, the pancreatic cancer patient group, the bile duct cancer patient group, the stomach cancer patient group, the esophageal cancer patient group, the colorectal cancer patient group, and the benign pancreaticobiliary disease patient group as negative sample groups. The discriminant performance of the selected polynucleotides was validated using independent samples.

Most of polynucleotides consisting of the nucleotide sequences represented by these SEQ ID NOs (SEQ ID NOs: 1 to 224 and 714 to 729 corresponding to the miRNA markers of Table 1) or complementary sequences thereof mentioned above were able to provide relatively high accuracy, sensitivity, and specificity in the determination of the presence or absence of liver cancer, and furthermore, were able to specifically discriminate liver cancer from other cancers. For example, among the combinations of a plurality of polynucleotides selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 2, 3, 5, 7, 9, 12, 17, 20, 22, 27, 28, 29, 38, 39, 44, 46, 48, 51, 54, 61, 76, 89, 93, 101, 109, 116, 123, 132, 134, 136, 148, 150, 151, 155, 157, 164, 166, 167, 172, 180, 186, 188, 189, 197, 198, 214, 216, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728 and 729 or complementary sequences thereof (the cancer type-specific polynucleotide group 1) as polynucleotides capable of specifically binding to target markers, combinations comprising at least one or more polynucleotide(s) selected from the group consisting of polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1, 3, 7, 9, 22, 38, 44, 134, 148, 155, 157, 164, 167, 172, 214, 714, 715, 716, and 717 or complementary

sequences thereof (the cancer type-specific polynucleotide group 2) were able to specifically discriminate liver cancer from other cancers with high accuracy.

The number of the polynucleotides with cancer type specificity in the combination mentioned above can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more for the combination. The combinations of 4 or more polynucleotides were able to exhibit discriminant accuracy of 90% or higher.

Specifically, the discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof is shown in Table 8-1. In Table 8-1, "SEQ ID NO" represents one polynucleotide or a combination of a plurality of polynucleotides used with the number of SEQ ID NO: (the same holds true for Tables 8-2 to 8-19). The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited accuracy of 71.2% in the training cohort and accuracy of 73.2% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited the highest accuracy of 88.1% in the training cohort and accuracy of 90% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited the highest accuracy of 90.2% in the training cohort and accuracy of 90.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 1 or a complementary sequence thereof exhibited the highest accuracy of 92.3% in the training cohort and accuracy of 93.2% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof is shown in Table 8-2. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited accuracy of 78.7% in the training cohort and accuracy of 73.2% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited the highest accuracy of 88.7% in the training cohort and accuracy of 87.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited the highest accuracy of 91.8% in the training cohort and accuracy of 87.9% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 3 or a complementary sequence thereof exhibited the highest accuracy of 92.9% in the training cohort and accuracy of 93.2% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof is shown in Table 8-3. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof exhibited accuracy of 85.5% in the training cohort and accuracy of 84.7% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof exhibited the highest accuracy of 91.5% in the training cohort and accuracy of 90.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof exhibited the highest accuracy of 93.7% in the training cohort and accuracy of 92.1% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 7 or a complementary sequence thereof exhibited the highest accuracy of 94.4% in the training cohort and accuracy of 92.6% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 9 or a complementary sequence thereof is shown in Table 8-4. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 9 or a complementary sequence thereof exhibited accuracy of 59.7% in the training cohort and accuracy of 59.5% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 9 or a complementary sequence thereof exhibited the highest accuracy of 86% in the training cohort and accuracy of 81.1% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 9 or a complementary sequence thereof exhibited the highest accuracy of 91.8% in the training cohort and accuracy of 84.7% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 9 or a complementary sequence thereof exhibited the highest accuracy of 94.7% in the training cohort and accuracy of 92.1% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 22 or a complementary sequence thereof is shown in Table 8-5. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 22 or a complementary sequence thereof exhibited accuracy of 76.5% in the training cohort and accuracy of 78.9% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 22 or a complementary sequence thereof exhibited the highest accuracy of 85.8% in the training cohort and accuracy of 84.7% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 22 or a complemen-

tary sequence thereof exhibited the highest accuracy of 91.3% in the training cohort and accuracy of 91.6% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 22 or a complementary sequence thereof exhibited the highest accuracy of 93.7% in the training cohort and accuracy of 93.7% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 38 or a complementary sequence thereof is shown in Table 8-6. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 38 or a complementary sequence thereof exhibited accuracy of 65.5% in the training cohort and accuracy of 65.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 38 or a complementary sequence thereof exhibited the highest accuracy of 86.3% in the training cohort and accuracy of 84.2% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 38 or a complementary sequence thereof exhibited the highest accuracy of 92.3% in the training cohort and accuracy of 91.6% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 38 or a complementary sequence thereof exhibited the highest accuracy of 94.2% in the training cohort and accuracy of 92.1% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 44 or a complementary sequence thereof is shown in Table 8-7. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 44 or a complementary sequence thereof exhibited accuracy of 62.6% in the training cohort and accuracy of 62.1% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 44 or a complementary sequence thereof exhibited the highest accuracy of 90.5% in the training cohort and accuracy of 86.3% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 44 or a complementary sequence thereof exhibited the highest accuracy of 92.9% in the training cohort and accuracy of 91.1% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 44 or a complementary sequence thereof exhibited the highest accuracy of 93.7% in the training cohort and accuracy of 91.6% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 134 or a complementary sequence thereof is shown in Table 8-8. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 134 or a complementary sequence thereof exhibited accuracy of 53.4% in the training cohort and accuracy of 58.9% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 134 or a complementary sequence thereof exhibited the highest accuracy of 87.3% in the training cohort and accuracy of 84.2% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 134 or a complementary sequence thereof exhibited the highest accuracy of 92.9% in the training cohort and accuracy of 91.1% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 134 or a complementary sequence thereof exhibited the highest accuracy of 93.7% in the training cohort and accuracy of 92.1% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 148 or a complementary sequence thereof is shown in Table 8-9. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 148 or a complementary sequence thereof exhibited accuracy of 73.6% in the training cohort and accuracy of 75.3% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 148 or a complementary sequence thereof exhibited the highest accuracy of 86.3% in the training cohort and accuracy of 85.3% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 148 or a complementary sequence thereof exhibited the highest accuracy of 93.7% in the training cohort and accuracy of 91.6% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 148 or a complementary sequence thereof exhibited the highest accuracy of 93.7% in the training cohort and accuracy of 92.1% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 155 or a complementary sequence thereof is shown in Table 8-10. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 155 or a complementary sequence thereof exhibited accuracy of 60.8% in the training cohort and accuracy of 58.9% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 155 or a complementary sequence thereof exhibited the highest accuracy of 86.5% in the training cohort and accuracy of 85.8% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide

sequence represented by SEQ ID NO: 155 or a complementary sequence thereof exhibited the highest accuracy of 90.5% in the training cohort and accuracy of 91.6% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 155 or a complementary sequence thereof exhibited the highest accuracy of 93.4% in the training cohort and accuracy of 91.6% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 157 or a complementary sequence thereof is shown in Table 8-11. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 157 or a complementary sequence thereof exhibited accuracy of 70.3% in the training cohort and accuracy of 68.9% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 157 or a complementary sequence thereof exhibited the highest accuracy of 86.5% in the training cohort and accuracy of 83.2% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 157 or a complementary sequence thereof exhibited the highest accuracy of 91% in the training cohort and accuracy of 91.6% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 157 or a complementary sequence thereof exhibited the highest accuracy of 93.9% in the training cohort and accuracy of 92.6% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 164 or a complementary sequence thereof is shown in Table 8-12. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 164 or a complementary sequence thereof exhibited accuracy of 72.4% in the training cohort and accuracy of 65.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 164 or a complementary sequence thereof exhibited the highest accuracy of 87.6% in the training cohort and accuracy of 87.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 164 or a complementary sequence thereof exhibited the highest accuracy of 91.5% in the training cohort and accuracy of 92.1% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 164 or a complementary sequence thereof exhibited the highest accuracy of 92.6% in the training cohort and accuracy of 90.5% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 167 or a complementary sequence thereof is shown in Table 8-13. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 167 or a complementary sequence thereof exhibited accuracy of 62.1% in the training cohort and accuracy of 57.4% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 167 or a complementary sequence thereof exhibited the highest accuracy of 89.2% in the training cohort and accuracy of 87.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 167 or a complementary sequence thereof exhibited the highest accuracy of 92.1% in the training cohort and accuracy of 90% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 167 or a complementary sequence thereof exhibited the highest accuracy of 93.4% in the training cohort and accuracy of 91.1% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 172 or a complementary sequence thereof is shown in Table 8-14. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 172 or a complementary sequence thereof exhibited accuracy of 76.8% in the training cohort and accuracy of 75.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 172 or a complementary sequence thereof exhibited the highest accuracy of 86.3% in the training cohort and accuracy of 83.7% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 172 or a complementary sequence thereof exhibited the highest accuracy of 90.2% in the training cohort and accuracy of 90.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 172 or a complementary sequence thereof exhibited the highest accuracy of 92.1% in the training cohort and accuracy of 93.2% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 214 or a complementary sequence thereof is shown in Table 8-15. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 214 or a complementary sequence thereof exhibited accuracy of 69.5% in the training cohort and accuracy of 67.4% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 214 or a complementary sequence thereof exhibited the highest accuracy of 89.2% in the training cohort and accuracy of 87.9% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at

least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 214 or a complementary sequence thereof exhibited the highest accuracy of 91.5% in the training cohort and accuracy of 90.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 214 or a complementary sequence thereof exhibited the highest accuracy of 93.4% in the training cohort and accuracy of 92.6% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 714 or a complementary sequence thereof is shown in Table 8-16. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 714 or a complementary sequence thereof exhibited accuracy of 44.7% in the training cohort and accuracy of 46.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 714 or a complementary sequence thereof exhibited the highest accuracy of 90.2% in the training cohort and accuracy of 87.4% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 714 or a complementary sequence thereof exhibited the highest accuracy of 92.1% in the training cohort and accuracy of 91.1% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 714 or a complementary sequence thereof exhibited the highest accuracy of 94.4% in the training cohort and accuracy of 94.2% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 715 or a complementary sequence thereof is shown in Table 8-17. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 715 or a complementary sequence thereof exhibited accuracy of 64.2% in the training cohort and accuracy of 65.8% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 715 or a complementary sequence thereof exhibited the highest accuracy of 87.9% in the training cohort and accuracy of 86.8% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 715 or a complementary sequence thereof exhibited the highest accuracy of 91.8% in the training cohort and accuracy of 91.1% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 715 or a complementary sequence thereof exhibited the highest accuracy of 93.9% in the training cohort and accuracy of 93.2% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 716 or a complementary sequence thereof is shown in Table 8-18. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 716 or a complementary sequence thereof exhibited accuracy of 62.6% in the training cohort and accuracy of 58.9% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 716 or a complementary sequence thereof exhibited the highest accuracy of 90.2% in the training cohort and accuracy of 86.3% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 716 or a complementary sequence thereof exhibited the highest accuracy of 91.3% in the training cohort and accuracy of 91.6% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 716 or a complementary sequence thereof exhibited the highest accuracy of 93.7% in the training cohort and accuracy of 92.1% in the validation cohort.

The discriminant accuracy of the measurement using the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 717 or a complementary sequence thereof is shown in Table 8-19. The measurement using, alone (one), the polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 717 or a complementary sequence thereof exhibited accuracy of 70.3% in the training cohort and accuracy of 66.3% in the validation cohort. Also, for example, the measurement using the combinations of two polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 717 or a complementary sequence thereof exhibited the highest accuracy of 86.8% in the training cohort and accuracy of 84.7% in the validation cohort. Furthermore, for example, the measurement using the combinations of three polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 717 or a complementary sequence thereof exhibited the highest accuracy of 92.3% in the training cohort and accuracy of 90.5% in the validation cohort. Furthermore, for example, the measurement using the combinations of four polynucleotides comprising at least one polynucleotide consisting of the nucleotide sequence represented by SEQ ID NO: 717 or a complementary sequence thereof exhibited the highest accuracy of 93.1% in the training cohort and accuracy of 92.6% in the validation cohort.

The expression level measurement values of the nucleotide sequences represented by SEQ ID NOs: 7, 9, 27, and 148 were compared among 35 liver cancer patients, 99 healthy subjects, 72 pancreatic cancer patients, 61 bile duct cancer patients, 38 stomach cancer patients, 25 esophageal cancer patients, 35 colorectal cancer patients, and 16 benign pancreaticobiliary disease patients in the training cohort. As a result, a scatter diagram that significantly separated the discriminant score of the liver cancer patient group from the discriminant scores of the other groups was obtained in the training cohort (see the upper diagram of FIG. **4**). These results were also reproducible in the validation cohort (see the lower diagram of FIG. **4**).

TABLE 8-1

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1	71.2	94.3	68.9	73.2	100	70.5
1__155	88.1	91.4	87.8	90	88.2	90.2
1__7__155	90.2	88.6	90.4	90.5	88.2	90.8
1__7__9__148	92.3	91.4	92.4	93.2	100	92.5
1__9__155__172	91.3	94.3	91	91.6	94.1	91.3
1__9__148__155	90.2	91.4	90.1	90.5	100	89.6
1__155__172__715	91	91.4	91	93.2	100	92.5
1__155__164__715	90.8	94.3	90.4	93.7	100	93.1

TABLE 8-2

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
3	78.7	85.7	78	73.2	82.4	72.3
3__7	88.7	85.7	89	87.4	82.4	87.9
3__7__718	91.8	88.6	92.2	87.9	88.2	87.9
3__7__9__148	92.9	88.6	93.3	93.2	94.1	93.1
3__22__27__46	90.8	91.4	90.7	91.1	94.1	90.8
1__3__29__155	91	88.6	91.3	95.3	94.1	95.4
1__3__151__155	90.7	88.6	91	95.8	94.1	96
3__7__148__715	92.3	88.6	92.7	90	94.1	89.6

TABLE 8-3

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
7	85.5	85.7	85.5	84.7	82.4	85
7__148	91.5	85.7	92.1	90.5	88.2	90.8
7__9__148	93.7	91.4	93.9	92.1	100	91.3
7__28__148__717	94.2	91.4	94.5	92.1	100	91.3
7__9__148__186	93.4	91.4	93.6	91.6	94.1	91.3
7__148__172__715	92.1	88.6	92.4	92.6	100	91.9
7__9__148__723	93.4	91.4	93.6	92.1	100	91.3
7__9__28__148	94.4	91.4	94.8	92.6	100	91.9

TABLE 8-4

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
9	59.7	62.9	59.4	59.5	94.1	56.1
7__9	86	88.6	85.8	81.1	82.4	80.9
7__9__714	91.8	85.7	92.4	84.7	76.5	85.5
7__9__148__157	93.4	91.4	93.6	92.1	100	91.3
7__9__148__722	93.9	91.4	94.2	91.6	94.1	91.3
7__9__27__148	94.7	91.4	95	92.1	94.1	91.9
7__9__148__725	93.7	91.4	93.9	92.1	100	91.3
7__9__148__729	93.7	91.4	93.9	91.1	94.1	90.8

TABLE 8-5

	Training cohort			Validation cohort		
SEQ ID NO:	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
22	76.5	77.1	76.5	78.9	76.5	79.2
3__22	85.8	88.6	85.5	84.7	88.2	84.4

TABLE 8-5-continued

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
7_22_148	91.3	88.6	91.5	91.6	88.2	91.9
7_9_22_148	93.7	91.4	93.9	93.7	100	93.1
7_22_28_148	93.7	91.4	93.9	92.6	94.1	92.5
7_22_148_189	91.8	85.7	92.4	92.1	88.2	92.5
2_7_22_148	92.1	91.4	92.1	92.6	100	91.9
7_22_148_720	92.3	82.9	93.3	93.2	88.2	93.6

TABLE 8-6

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
38	65.5	51.4	67	65.8	76.5	64.7
7_38	86.3	85.7	86.3	84.2	82.4	84.4
7_38_148	92.3	88.6	92.7	91.6	94.1	91.3
7_9_38_148	94.2	91.4	94.5	92.1	100	91.3
7_38_51_148	93.1	88.6	93.6	91.6	94.1	91.3
7_38_148_718	92.9	88.6	93.3	92.6	94.1	92.5
7_38_148_216	92.3	88.6	92.7	93.2	94.1	93.1
7_38_148_728	91.5	88.6	91.8	92.1	94.1	91.9

TABLE 8-7

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
44	62.6	62.9	62.6	62.1	94.1	59
7_44	90.5	85.7	91	86.3	88.2	86.1
7_44_148	92.9	91.4	93	91.1	100	90.2
7_9_44_148	93.7	91.4	93.9	91.6	100	90.8
7_44_123_148	93.4	91.4	93.6	91.1	100	90.2
7_38_44_148	92.9	91.4	93	91.1	100	90.2
7_44_148_723	93.1	91.4	93.3	91.1	100	90.2
7_44_48_148	93.7	91.4	93.9	92.1	100	91.3

TABLE 8-8

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
134	53.4	45.7	54.2	58.9	64.7	58.4
7_134	87.3	85.7	87.5	84.2	76.5	85
7_134_148	92.9	88.6	93.3	91.1	100	90.2
7_9_134_148	93.7	91.4	93.9	92.1	100	91.3
7_134_148_724	93.4	88.6	93.9	93.7	94.1	93.6
7_22_134_148	92.3	91.4	92.4	93.7	100	93.1
7_134_148_189	92.9	88.6	93.3	91.6	100	90.8
7_134_148_714	92.6	85.7	93.3	90	94.1	89.6

TABLE 8-9

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
148	73.6	85.7	72.4	75.3	82.4	74.6
48_148	86.3	88.6	86	85.3	88.2	85
7_28_148	93.7	85.7	94.5	91.6	94.1	91.3
7_9_148_726	93.7	91.4	93.9	92.1	100	91.3

TABLE 8-9-continued

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
7_9_148_151	93.6	91.4	93.9	93.7	94.1	93.6
7_9_109_148	93.7	91.4	93.9	92.1	100	91.3
5_7_9_148	92.9	91.4	93	93.2	100	92.5
7_9_76_148	93.4	91.4	93.6	91.6	100	90.8

TABLE 8-10

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
155	60.8	65.7	60.3	58.9	64.7	58.4
7_155	86.5	85.7	86.6	85.8	82.4	86.1
7_148_155	90.5	85.7	91	91.6	88.2	91.9
7_9_148_155	93.4	91.4	93.6	91.6	100	90.8
7_38_148_155	93.4	88.6	93.9	93.2	94.1	93.1
1_9_155_167	90	94.3	89.5	92.6	100	91.9
1_3_155_715	89.7	88.6	89.8	93.2	100	92.5
1_3_38_155	90	88.6	90.1	93.7	94.1	93.6

TABLE 8-11

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
157	70.3	71.4	70.1	68.9	94.1	66.5
7_157	86.5	85.7	86.6	83.2	82.4	83.2
7_148_157	91	88.6	91.3	91.6	94.1	91.3
7_48_157_714	93.9	88.6	94.5	92.6	94.1	92.5
7_38_148_157	92.3	88.6	92.7	92.6	94.1	92.5
1_44_155_157	89.4	94.3	89	90.5	100	89.6
7_76_157_714	92.9	82.9	93.9	90.5	94.1	90.2
7_148_157_189	91.8	88.6	92.1	92.1	94.1	91.9

TABLE 8-12

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
164	72.4	82.9	71.3	65.8	76.5	64.7
7_164	87.6	85.7	87.8	87.4	88.2	87.3
7_148_164	91.5	85.7	92.1	92.1	94.1	91.9
7_9_148_164	92.3	91.4	92.4	91.1	94.1	90.8
7_76_164_714	91.3	85.7	91.8	94.2	94.1	94.2
7_38_164_714	92.6	82.9	93.6	90.5	82.4	91.3
7_38_148_164	92.3	88.6	92.7	91.6	94.1	91.3
1_7_164_714	90.5	85.7	91	94.2	94.1	94.2

TABLE 8-13

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
167	62.1	68.6	61.4	57.4	70.6	56.1
7_167	89.2	85.7	89.5	87.4	82.4	87.9
7_148_167	92.1	85.7	92.7	90	88.2	90.2
7_9_148_167	93.1	91.4	93.3	92.6	100	91.9
1_7_167_714	92.6	85.7	93.3	94.7	100	94.2
7_151_167_714	92.9	85.7	93.6	92.1	88.2	92.5

TABLE 8-13-continued

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
7__148__167__189	92.9	85.7	93.6	92.6	88.2	93.1
7__28__167__714	93.4	85.7	94.2	91.1	88.2	91.3

TABLE 8-14

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
172	76.8	91.4	75.4	75.8	82.4	75.1
7__172	86.3	85.7	86.3	83.7	76.5	84.4
1__155__172	90.2	94.3	89.8	90.5	88.2	90.8
7__9__148__172	92.1	91.4	92.1	93.2	94.1	93.1
7__150__172__714	92.1	85.7	92.7	92.1	94.1	91.9
7__172__714__715	91.3	82.9	92.2	92.1	94.1	91.9
7__38__155__172	91.3	91.4	91.3	89.5	76.5	90.8
1__2__155__172	89.7	94.3	89.2	91.6	94.1	91.3

TABLE 8-15

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
214	69.5	77.1	68.7	67.4	64.7	67.6
7__214	89.2	85.7	89.5	87.9	82.4	88.4
7__148__214	91.5	85.7	92.1	90.5	88.2	90.8
7__9__148__214	93.4	91.4	93.6	92.6	100	91.9
7__148__189__214	92.6	85.7	93.3	92.1	88.2	92.5
2__7__148__214	92.1	91.4	92.1	93.7	100	93.1
1__7__214__714	91	88.6	91.3	94.7	94.1	94.8
7__39__148__214	92.1	88.6	92.4	90	88.2	90.2

TABLE 8-16

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
714	44.7	31.4	46.1	46.8	41.2	47.4
7__714	90.2	82.9	91	87.4	82.4	87.9
7__157__714	92.1	85.7	92.7	91.1	94.1	90.8
7__9__148__714	93.4	91.4	93.6	92.1	94.1	91.9
7__54__148__714	93.4	88.6	93.9	95.3	94.1	95.4
7__148__151__714	94.4	88.6	95	94.2	94.1	94.2
7__38__148__714	93.4	85.7	94.2	93.2	94.1	93.1
7__28__148__714	93.9	85.7	94.8	93.7	94.1	93.6

TABLE 8-17

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
715	64.2	71.4	63.5	65.8	76.5	64.7
7__715	87.9	85.7	88.1	86.8	94.1	86.1
7__148__715	91.8	88.6	92.1	91.1	100	90.2
2__7__148__715	93.1	91.4	93.3	91.6	100	90.8
7__9__148__715	93.9	91.4	94.2	93.2	100	92.5
7__17__148__715	93.7	91.4	93.9	91.1	100	90.2

TABLE 8-17-continued

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
7_38_148_715	92.6	88.6	93	91.1	100	90.2
7_148_715_725	92.3	88.6	92.7	91.6	100	90.8

TABLE 8-18

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
716	62.6	80	60.9	58.9	70.6	57.8
7_716	90.2	85.7	90.7	86.3	76.5	87.3
7_148_716	91.3	85.7	91.8	91.6	88.2	91.9
7_9_148_716	93.7	91.4	93.9	92.1	100	91.3
7_148_714_716	93.1	85.7	93.9	92.1	88.2	92.5
2_7_148_716	91.8	91.4	91.8	92.6	100	91.9
7_38_148_716	92.6	88.6	93	92.1	94.1	91.9
7_148_715_716	91.8	88.6	92.1	91.6	100	90.8

TABLE 8-19

SEQ ID NO:	Training cohort Accuracy (%)	Sensitivity (%)	Specificity (%)	Validation cohort Accuracy (%)	Sensitivity (%)	Specificity (%)
717	70.3	85.7	68.7	66.3	82.4	64.7
7_717	86.8	85.7	86.9	84.7	82.4	85
7_148_717	92.3	85.7	93	90.5	88.2	90.8
7_9_148_717	93.1	91.4	93.3	92.6	100	91.9
7_38_148_717	92.3	88.6	92.7	91.6	94.1	91.3
7_27_148_717	93.1	85.7	93.9	91.6	88.2	91.9
7_44_148_717	93.1	91.4	93.3	92.1	100	91.3
7_148_715_717	92.6	88.6	93	91.1	100	90.2

Comparative Example 1

Liver Cancer Discriminant Performance of Existing Tumor Marker in Blood

The concentrations of the existing tumor markers AFP, CEA, CA19-9, and PIVKA-II for detecting liver cancer in blood were measured in the training cohort and the validation cohort obtained in Reference Example 1. When the concentrations of these tumor markers in blood are higher than the reference values described in Non-Patent Literature 5 (AFP: 10 ng/mL, CEA: 5 ng/mL, CA19-9: 37 U/mL, PIVKA-II: 40 mAU/mL), subjects are usually suspected of having cancer. Thus, whether or not the concentration of each tumor marker in blood exceeded its reference value was determined for each sample, and the results were assessed for the ability of these tumor markers to detect cancer in liver cancer patients. The sensitivity of each existing marker in the training cohort and the validation cohort was calculated. The results are shown in Table 5. The sensitivity of AFP, which had the highest sensitivity among the 4 existing tumor markers measured, was as low as 56.3% in the training cohort, and was as low as 53.3% in the validation cohort, demonstrating that neither of the markers are useful in the detection of liver cancer (Table 5).

On the other hand, as shown above in Tables 3 and 6 of Examples 1 and 2, it can be concluded that all of the polynucleotides consisting of the nucleotide sequences represented by SEQ ID NOs: 1 to 183 have combinations of 1 or 2 polynucleotides exhibiting sensitivity beyond the existing liver cancer markers and thus serve as excellent diagnosis markers.

As shown in these Examples and Comparative Example, the kit, etc., and the method of the present invention can detect liver cancer with higher sensitivity than the existing tumor markers and therefore permit early detection of liver cancer. As a result, surgical resection having high potentiality of radical cure can be applied, leading to drastic improvement in survival rate.

INDUSTRIAL APPLICABILITY

According to the present invention, liver cancer can be effectively detected by a simple and inexpensive method. This enables early detection, diagnosis and treatment of liver cancer. The method of the present invention can detect liver cancer with limited invasiveness using the blood of a patient and therefore allows liver cancer to be detected conveniently and rapidly.

All publications, patents, and patent applications cited herein are incorporated herein by reference in their entirety.

SEQUENCE LISTING

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<400> SEQUENCE: 120

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uucagauccc agcggugccu cu 22

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uggggcugg gaugggccau ggu 23

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ccaggaggcg gaggaggugg ag 22

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cgggggcggg gccgaagcgc g 21

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<400> SEQUENCE: 128

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ccccgccacc gccuugg 17

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<400> SEQUENCE: 130

cagcaggga gagagaggag uc 22

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uggggagcgg cccccgggug gg 22

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uaggggggcgg cuuguggagu gu 22

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gugaggaggg gcuggcaggg ac 22

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<400> SEQUENCE: 140

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aggcaggggc uggugcuggg cggg 24

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<400> SEQUENCE: 145

cgcgccgggc ccggguu 17

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auauacaggg ggagacucuu au 22

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<400> SEQUENCE: 156

cguggaggac gaggaggagg c 21

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gagacugggg uggggcc 17

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ggggggccgau acacuguacg aga 23

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gcgggggcugg gcgcgcg 17

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<400> SEQUENCE: 160

uguaggcaug aggcagggcc cagg 24

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<400> SEQUENCE: 161

ugggggagga aggacaggcc au 22

<210> SEQ ID NO 162
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gcugcgggcu gcggucaggg cg 22

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uuagggagua gaaggguggg gag 23

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gugaacgggc gccaucccga gg 22

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ggggggugug gagccagggg gc 22

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aucacauugc cagggauuac c 21

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<400> SEQUENCE: 171

ucacaccugc cucgcccccc 20

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gaacgccugu ucuugccagg ugg 23

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<400> SEQUENCE: 173

ucugcccccu ccgcugcugc ca 22

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<400> SEQUENCE: 174

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uauugcacuc gucccggccu cc 22

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<400> SEQUENCE: 178

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aggcacggug ucagcaggc 19

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acaggugagg uucuugggag cc 22

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agggacggga cgcggugcag ug 22

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<400> SEQUENCE: 182

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<400> SEQUENCE: 183

aggcggggcg ccgcgggacc gc 22

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<400> SEQUENCE: 184

uaggggcagc agaggaccug gg 22

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<400> SEQUENCE: 185

ugugggacug caaaugggag 20

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aaggggcugg gggagcaca 19

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<400> SEQUENCE: 187

gugaaggccc ggcggaga 18

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<400> SEQUENCE: 188

ugguggagga agagggcagc uc 22

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<400> SEQUENCE: 189

gggggggcag gaggggcuca ggg 23

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 190

cacacaggaa aagcggggcc cug 23

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<400> SEQUENCE: 191

uggggcggag cuuccggag 19

<210> SEQ ID NO 192
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<400> SEQUENCE: 192

ugaggcgggg gggcgagc 18

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<400> SEQUENCE: 193

accacugcac uccagccuga g 21

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guggguacgg cccagugggg gg 22

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<400> SEQUENCE: 195

cggggcggca ggggccuc 18

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<400> SEQUENCE: 196

caggaggcag ugggcgagca gg 22

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<400> SEQUENCE: 197

uagggggugg caggcuggcc 20

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<212> TYPE: RNA
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<400> SEQUENCE: 198

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<400> SEQUENCE: 199

caggggcugg gguuucaggu ucu 23

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<400> SEQUENCE: 200

accaggaggc ugaggccccu 20

<210> SEQ ID NO 201
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<400> SEQUENCE: 201

cggggcagcu caguacagga u 21

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<400> SEQUENCE: 202

gggugcgggc cggcgggg 18

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<400> SEQUENCE: 203

cugggagagg guuguuuacu cc 22

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<400> SEQUENCE: 204

cgcgggucgg ggucugcagg 20

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<400> SEQUENCE: 205

aaggggcagg gacggguggc cc 22

<210> SEQ ID NO 206

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<211> LENGTH: 22
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<400> SEQUENCE: 206

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<400> SEQUENCE: 207

cgggcugucc ggaggggucg gcu 23

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<400> SEQUENCE: 208

gggaccaucc ugccugcugu gg 22

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<400> SEQUENCE: 209

guaggggagg uugggccagg ga 22

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<400> SEQUENCE: 210

ugggggagug cagugauugu gg 22

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<400> SEQUENCE: 211

acucaaacug ugggggcacu 20

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<400> SEQUENCE: 212

aggggggcggg cuccggcg 18

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<400> SEQUENCE: 213

agugggaggc cagggcacgg ca 22

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<210> SEQ ID NO 214
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<400> SEQUENCE: 214

uggggagcc augagauaag agca 24

<210> SEQ ID NO 215
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<400> SEQUENCE: 215

uggcucaguu cagcaggaac ag 22

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<400> SEQUENCE: 216

gugaguggga gccccagugu gug 23

<210> SEQ ID NO 217
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<400> SEQUENCE: 217

gccggacaag agggagg 17

<210> SEQ ID NO 218
<211> LENGTH: 22
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<400> SEQUENCE: 218

ggaggaaccu uggagcuucg gc 22

<210> SEQ ID NO 219
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<400> SEQUENCE: 219

ugggaauggg gguaagggcc 20

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ggaggccggg gugggggcggg gcgg 24

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<400> SEQUENCE: 221

gggaaaagga agggggagga 20

<210> SEQ ID NO 222
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<400> SEQUENCE: 222

agugggagga caggaggcag gu 22

<210> SEQ ID NO 223
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<400> SEQUENCE: 223

guuugcacgg gugggccuug ucu 23

<210> SEQ ID NO 224
<211> LENGTH: 19
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<400> SEQUENCE: 224

ggggagcgag gggcggggc 19

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<211> LENGTH: 84
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 225

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cccgcacucu cgcucugggc ccgc 84

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 226

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g 61

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<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 227

cauuggaggg uguggaagac aucugggcca acucugaucu cuucaucuac cccccag 57

<210> SEQ ID NO 228
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 228

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uucaccgcgg ccg 73

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<212> TYPE: RNA
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<400> SEQUENCE: 229

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agaggugggg acugagccuu aguugg 86

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<211> LENGTH: 85
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<400> SEQUENCE: 230

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ugugcggaua cggggcugga ggccu 85

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<211> LENGTH: 109
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 231

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ggugggguucu ggcuggucag augggagugg acagagaccc gggguccuc 109

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<400> SEQUENCE: 232

augagcgggu gggagcagau cuuauugaga guuccuucuc cugcuccuga uugucuuccc 60

ccacccucac ag 72

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<211> LENGTH: 61
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 233

ucucguuuga ucucggaagc uaagcagggu ugggccuggu uaguacuugg augggaaacu 60

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<211> LENGTH: 53
<212> TYPE: RNA
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<400> SEQUENCE: 234

guuugaucuc ggaagcuaag cagggucggg ccugguuagu acuuggaugg gag 53

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 235

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 236

cguggugagg auauggcagg gaaggggagu uucccucuau ucccuucccc ccaguaaucu 60

ucaucaug 68

<210> SEQ ID NO 237
<211> LENGTH: 61
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 237

ucggcuggcg gggguagagc uggcugcagg cccggccccu cucagcugcu gcccucucca 60

g 61

<210> SEQ ID NO 238
<211> LENGTH: 55
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 238

ccggauccga gucacggcac caaauuucau gcguguccgu gugaagagac cacca 55

<210> SEQ ID NO 239
<211> LENGTH: 68
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 239

ugcccaggcu ggagcgagug caguggugca gucaguccua gcucacugca gccucgaacu 60

ccugggcu 68

<210> SEQ ID NO 240
<211> LENGTH: 87
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 240

gugaggcggg gccaggaggg uguguggcgu gggugcugcg gggccgucag ggugccugcg 60

ggacgcucac cuggcuggcc cgcccag 87

<210> SEQ ID NO 241
<211> LENGTH: 68
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 241

gugcaaagag caggaggaca ggggauuuau cucccaaggg aggucccug auccuaguca 60

cggcacca 68

<210> SEQ ID NO 242
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 242

ggcuacaguc uuucuucaug ugacucgugg acuucccuuu gucauccuau gccugagaau 60

auaugaagga ggcugggaag gcaaagggac guucaauugu caucacuggc 110

<210> SEQ ID NO 243
<211> LENGTH: 49
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 243

uucccagcca acgcaccaaa aaugauaugg gucuguuguc uggagaaac 49

<210> SEQ ID NO 244
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 244

ggggcugggg gugugggggag agagagugca cagccagcuc agggauuaaa gcucuuucuc 60

ucucucucuc ucccacuucc cugcag 86

<210> SEQ ID NO 245
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 245

cugguguuug aggcgaugug gggauguaga gacaacuucc cagucucauu uccucauccu 60

gccaggccac cau 73

<210> SEQ ID NO 246
<211> LENGTH: 60
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 246

caaggugggg gagaugggggg uugaacuuca uuucucaugc ucaucccccau cuccuuucag 60

<210> SEQ ID NO 247
<211> LENGTH: 115
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 247

ggugccgagg gccguccggc auccuaggcg ggucgcugcg guaccucccu ccugucugug 60

gcgggugggau cccguggccg uguuuuccug guggcccggc cgugccugag guuuc 115

<210> SEQ ID NO 248
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 248

gagucugagg gacccaggac aggagaaggc cuauggugau uugcauucuu ccugcccugg 60

cuccauccuc ag 72

<210> SEQ ID NO 249
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 249

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gcgucaagau ggcggcgggg agguaggcag agcaggacgc cgcugcugcc gccgccaccg 60

ccgccuccgc uccagucgcc 80

<210> SEQ ID NO 250
<211> LENGTH: 66
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 250

ccgagugggg cggggcaggu cccugcaggg acugugacac ugaaggaccu gcaccuucgc 60

ccacag 66

<210> SEQ ID NO 251
<211> LENGTH: 62
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 251

gcuggggguc ccccgacagu guggagcugg ggccgggucc cggggagggg gguucugggc 60

ag 62

<210> SEQ ID NO 252
<211> LENGTH: 65
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 252

gagggugggc gagggcggcu gagcggcucc auccccggc cugcucaucc cccucgcccu 60

cucag 65

<210> SEQ ID NO 253
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 253

cgccugagcg ugcagcagga caucuuccug accugguaau aauuagguga gaaggauggu 60

ugggggcggu cggcguaacu caggga 86

<210> SEQ ID NO 254
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 254

gcuacgggga gcggggagga agugggcgcu gcuucugcgu uaucuggaag gagcagccca 60

cuccuguccu gggcucugug gu 82

<210> SEQ ID NO 255
<211> LENGTH: 87
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 255

guguggccgg caggcgggug ggcgggggcg gccgguggga accccgcccc gccccgcgcc 60

cgcacucacc cgcccgucuc cccacag 87

<210> SEQ ID NO 256
<211> LENGTH: 102

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<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 256

uguguucccu auccuccuua ugucccaccc ccacuccugu uugaauauuu caccagaaac 60

aggagugggg ggugggacgu aaggaggaug ggggaaagaa ca 102

<210> SEQ ID NO 257
<211> LENGTH: 69
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 257

ccgggcaggc agguguaggg uggagcccac uguggcuccu gacucagccc ugcugccuuc 60

accugccag 69

<210> SEQ ID NO 258
<211> LENGTH: 93
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 258

gcuuguuggg gauuggguca ggccaguguu caagggcccc uccucuagua cucccuguuu 60

guguucugcc acugacugag cuucucccca cag 93

<210> SEQ ID NO 259
<211> LENGTH: 88
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 259

gugggccag gcgguggugg gcacugcugg ggugggcaca gcagccaugc agagcgggca 60

uuugaccccg ugccacccuu uuccccag 88

<210> SEQ ID NO 260
<211> LENGTH: 63
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 260

aauggguggg ugcugguggg agccgugccc uggccacuca uucggcucuc ucccucaccc 60

uag 63

<210> SEQ ID NO 261
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 261

cuugggaaug gcaaggaaac cguuaccauu acugaguuua guaaugguaa ugguucucuu 60

gcuauaccca ga 72

<210> SEQ ID NO 262
<211> LENGTH: 81
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 262

uagaggcagu uucaacagau guguagacuu uugauaugag aaauugguuu caaaaucagg 60

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agucggggcu uuacugcuuu u 81

<210> SEQ ID NO 263
<211> LENGTH: 83
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 263

aauagagggu gcacaggcac gggagcucag gugaggcagg gagcugagcu caccugaccu 60

cccaugccug ugcacccucu auu 83

<210> SEQ ID NO 264
<211> LENGTH: 96
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 264

cucgggaggg gcgggagggg ggucccggu gcucggaucu cgagggugcu uauuguucgg 60

uccgagccug ggucucccuc uucccccaa cccccc 96

<210> SEQ ID NO 265
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 265

ugagcuguug gauucggggc cguagcacug ucugagaggu uuacauuucu cacagugaac 60

cggucucuuu uucagcugcu uc 82

<210> SEQ ID NO 266
<211> LENGTH: 66
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 266

gggcaugggg agguguggag ucagcauggg gcuaggaggc cccgcgcuga cccgccuucu 60

ccgcag 66

<210> SEQ ID NO 267
<211> LENGTH: 89
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 267

ucuccguuua ucccaccacu gccaccauua uugcuacugu ucagcaggug cugcuggugg 60

ugauggugau agucuggugg gggcggugg 89

<210> SEQ ID NO 268
<211> LENGTH: 81
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 268

cauccuccuu acgucccacc ccccacuccu guuucuggug aaauauucaa acaggagugg 60

gggugggaca uaaggaggau a 81

<210> SEQ ID NO 269
<211> LENGTH: 79
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 269

cucgaggugc ugggggacgc gugagcgcga gccgcuuccu cacggcucgg ccgcggcgcg 60

uagcccccgc cacaucggg 79

<210> SEQ ID NO 270
<211> LENGTH: 99
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 270

gcaagggaca gggagggucg uggcgacacu cgcgccagcu cccgggacgg cugggcucgg 60

gcuggucgcc gaccuccgac ccuccacuag augccuggc 99

<210> SEQ ID NO 271
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 271

cgggaaugcc gcggcgggga cggcgauugg uccguaugug uggugccacc ggccgccggc 60

uccgccccgg cccccgcccc 80

<210> SEQ ID NO 272
<211> LENGTH: 71
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 272

ugaccacccc cgggcaaaga ccugcagauc cccuguuaga gacgggccca ggacuuugug 60

cggggugccc a 71

<210> SEQ ID NO 273
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 273

aggacccuuc cagagggccc ccccucaauc cuguugugcc uaauucagag gguuggggugg 60

aggcucuccu gaagggcucu 80

<210> SEQ ID NO 274
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 274

ggaugauaag uuaugggcu ucuguagaga uuucuaugag aacaucucua aggaacuccc 60

ccaaacugaa uuc 73

<210> SEQ ID NO 275
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 275

aaccccgggc cggaggucaa gggcgucgcu ucucccuaau guugccucuu uuccacggcc 60

ucag 64

<210> SEQ ID NO 276
<211> LENGTH: 94
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 276

auaaaggaag uuaggcugag gggcagagag cgagacuuuu cuauuuucca aaagcucggu 60

cugaggcccc ucagucuugc uuccuaaccc gcgc 94

<210> SEQ ID NO 277
<211> LENGTH: 97
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 277

cccgggaccu ugguccaggc gcuggucugc guggugcucg gguggauaag ucugaucuga 60

gcaccacaca ggccgggcgc cgggaccaag ggggcuc 97

<210> SEQ ID NO 278
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 278

uacaggccgg ggcuuugggu gagggacccc cggagucugu cacggucuca ccccaacucu 60

gccccag 67

<210> SEQ ID NO 279
<211> LENGTH: 69
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 279

ggcccucggg ccuggggguug ggggagcucu guccugucuc acucauugcu ccuccccugc 60

cuggcccag 69

<210> SEQ ID NO 280
<211> LENGTH: 92
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 280

gucagugucu gggcggacag cugcaggaaa gggaagacca aggcuugcug ucuguccagu 60

cugccacccu acccugucug uucuugccac ag 92

<210> SEQ ID NO 281
<211> LENGTH: 71
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 281

gugucugugc cggucccagg agaaccugca gaggcaucgg gucagcggug cuccugcggg 60

ccgacacuca c 71

<210> SEQ ID NO 282
<211> LENGTH: 79
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 282

cagccugggg aaggcuuggc agggaagaca caugagcagu gccuccacuu cacgccucuc 60

ccuugucucc uuucccuag 79

<210> SEQ ID NO 283
<211> LENGTH: 71
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 283

ggugaguggg agccgguggg gcuggaguaa gggcacgccc ggggcugccc caccugcuga 60

ccacccuccc c 71

<210> SEQ ID NO 284
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 284

aagcaagacu gaggggccuc agaccgagcu uuuggaaaau agaaaagucu cgcucucugc 60

cccucagccu aacuu 75

<210> SEQ ID NO 285
<211> LENGTH: 96
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 285

gcucuggggc gugccgccgc cgucgcugcc accucccccua ccgcuagugg aagaagaugg 60

cggaaggcgg agcggcggau cuggacaccc agcggu 96

<210> SEQ ID NO 286
<211> LENGTH: 87
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 286

cccucaucuc ugggcagggg cuuauuguag gagucucuga agagagcugu ggacugaccu 60

gcuuuaaccc uuccccaggu ucccauu 87

<210> SEQ ID NO 287
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 287

ccagaccccu ggggcugggc aggcggaaag aggucugaac ugccucugcc uccuuggucu 60

ccggcag 67

<210> SEQ ID NO 288
<211> LENGTH: 68
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 288

gaauggaaga agaaggcggu cggucugcgg gagccaggcc gcagagccau ccgccuucug 60

uccauguc 68

<210> SEQ ID NO 289

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<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 289

accuuuccag cucaucccac cucugccacc aaaacacuca ucgcgggguc agagggagug 60

ccaaaaaagg uaa 73

<210> SEQ ID NO 290
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 290

ggcgagggga ggcgcaggcu cggaaaggcg cgcgaggcuc caggcuccuu cccgauccac 60

cgcucuccuc gcu 73

<210> SEQ ID NO 291
<211> LENGTH: 61
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 291

aacugcgggg ccagagcaga gagcccuugc acaccaccag ccucuccucc cugugcccca 60

g 61

<210> SEQ ID NO 292
<211> LENGTH: 65
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 292

gagaaugggg ggacagaugg agaggacaca ggcuggcacu gaggucccu ccacuuuccu 60

ccuag 65

<210> SEQ ID NO 293
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 293

gaaggcgagg gguagaagag cacaggggu cugauaaacc cuucugccug cauucuacuc 60

ccag 64

<210> SEQ ID NO 294
<211> LENGTH: 62
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 294

gugggucucg caucaggagg caaggccagg acccgcugac ccaugccucc ugccgcgguc 60

ag 62

<210> SEQ ID NO 295
<211> LENGTH: 89
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 295

accuccggga cggcugggcg ccggcggccg ggagauccgc gcuuccugaa ucccggccgg 60

cccgcccggc gcccguccgc ccgcgggguc 89

<210> SEQ ID NO 296
<211> LENGTH: 69
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 296

guggguaggg uuuggggggag agcgugggcu gggguucagg gacacccucu caccacugcc 60

cucccacag 69

<210> SEQ ID NO 297
<211> LENGTH: 62
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 297

ccuucugcgg cagagcuggg gucaccagcc cucauguacu ugugacuucu ccccugccac 60

ag 62

<210> SEQ ID NO 298
<211> LENGTH: 66
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 298

ucaagacggg gagucaggca gugguggaga uggagagccc ugagccucca cucuccuggc 60

ccccag 66

<210> SEQ ID NO 299
<211> LENGTH: 93
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 299

ggcgcuuuug ugcgcgcccg ggucuguugg ugcucagagu guggucaggc ggcucggacu 60

gagcaggugg gugcggggcu cggaggaggc ggc 93

<210> SEQ ID NO 300
<211> LENGTH: 55
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 300

gggggcuggg gcgcggggag gugcuagguc ggccucggcu cccgcgccgc acccc 55

<210> SEQ ID NO 301
<211> LENGTH: 93
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 301

uacuuauggc accccacucc ugguaccaua gucauaaguu aggagauguu agagcuguga 60

guaccaugac uuaagugugg uggcuuaaac aug 93

<210> SEQ ID NO 302
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 302

aguucagggc cgaagggugg aagcugcugg ugcucaucuc agccucugcc cuuggccucc 60

ccag 64

<210> SEQ ID NO 303
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 303

guggguacgg cccagugggg gggagaggga cacgcccugg gcucugccca gggugcagcc 60

ggacugacug agccccugug ccgcccccag 90

<210> SEQ ID NO 304
<211> LENGTH: 51
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 304

agagaugaag cgggggggcg gggucuugcu cuauugccua cgcugaucuc a 51

<210> SEQ ID NO 305
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 305

accuguaggu gacagucagg ggcggggugu gguggggcug gggcuggccc ccuccucaca 60

ccucuccugg caucgccccc ag 82

<210> SEQ ID NO 306
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 306

uguauccuug aauggauuuu uggagcagga guggacaccu gacccaaagg aaaucaaucc 60

auaggcuagc aau 73

<210> SEQ ID NO 307
<211> LENGTH: 63
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 307

ugguggcggc gguaguuaug ggcuucucuu ucucaccagc agccccuggg ccgccgccuc 60

ccu 63

<210> SEQ ID NO 308
<211> LENGTH: 68
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 308

cucaggcuca guggugcaug cuuauagucc cagccacucu ggaggcugaa ggaagauggc 60

uugagccu 68

<210> SEQ ID NO 309
<211> LENGTH: 80

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<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 309

cgugugagcc cgcccugugc ccggcccacu ucugcuuccu cuuagcgcag gagggguccc 60

gcacugggag gggcccucac 80

<210> SEQ ID NO 310
<211> LENGTH: 61
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 310

gagggcagcg uggguguggc ggaggcaggc gugaccguuu gccgcccucu cgcugcucua 60

g 61

<210> SEQ ID NO 311
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 311

ugagaggccg caccuugccu ugcugcccgg gccgugcacc cgugggcccc agggcgacgc 60

ggcgggggcg gcccuagcga 80

<210> SEQ ID NO 312
<211> LENGTH: 102
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 312

gcuuaucgag gaaaagaucg agguggguug gggcgggcuc uggggauuug gucucacagc 60

ccggauccca gcccacuuac cuugguuacu cuccuuccuu cu 102

<210> SEQ ID NO 313
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 313

uuugguacuu aaagagagga uacccuuugu auguucacuu gauuaauggc gaauauacag 60

ggggagacuc ucauuugcgu aucaaa 86

<210> SEQ ID NO 314
<211> LENGTH: 63
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 314

cuugcccggg agaaggaggu ggccuggaga gcugcugucu ccagccgccg ccugucucca 60

cag 63

<210> SEQ ID NO 315
<211> LENGTH: 100
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 315

agcucagggc ggcugcgcag agggcuggac ucagcggcgg agcuggcugc uggccucagu 60

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ucugccucug uccagguccu ugugacccgc ccgcucuccu 100

<210> SEQ ID NO 316
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 316

gugggcgggg gcaggugugu gguggguggu ggccugcggu gagcagggcc cucacaccug 60

ccucgccccc cag 73

<210> SEQ ID NO 317
<211> LENGTH: 137
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 317

agccagacaa gagggucaug gggagucacu gucaacccag agcaggcacu gccccugcga 60

ccagccuggg gcaucgguug gggugcaggg gucugcuggu gaugcuuucc aucucuuugc 120

uuuguccuga uuguagc 137

<210> SEQ ID NO 318
<211> LENGTH: 85
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 318

ggccugggua ggcuugcaug ggggacuggg aagagaccau gaacagguua guccagggag 60

uucucaucaa gccuuuacuc aguag 85

<210> SEQ ID NO 319
<211> LENGTH: 68
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 319

gacucggcug cgguggacaa guccggcucc agaaccugga caccgcucag ccggccgcgg 60

cagggguc 68

<210> SEQ ID NO 320
<211> LENGTH: 69
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 320

gaggagggga ggugugcagg gcuggggguca cugacucugc uuccccugcc cugcauggug 60

uccccacag 69

<210> SEQ ID NO 321
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 321

gaggcacugg guaggugggg cuccagggcu ccugacaccu ggaccucucc uccccaggcc 60

caca 64

<210> SEQ ID NO 322
<211> LENGTH: 65

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<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 322

gggugcucgg ggcaggcggc ugggagcggc ccucacauug auggcuccug ccaccuccuc 60

cgcag 65

<210> SEQ ID NO 323
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 323

auucuaggug gggagacuga cggcuggagg cccauaagcu gucuaaaacu ucggccccca 60

gauuucuggu cuccccacuu cagaac 86

<210> SEQ ID NO 324
<211> LENGTH: 62
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 324

uggccuaggg ggcggcuugu ggaguguaug ggcugagccu ugcucugcuc ccccgccccc 60

ag 62

<210> SEQ ID NO 325
<211> LENGTH: 59
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 325

ggggccaggc agggaggugg gaccaugggg gccuugcugu gugaccaccg uuccugcag 59

<210> SEQ ID NO 326
<211> LENGTH: 66
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 326

agcagcccuc ggcggcccgg ggggcgggcg gcggugcccg ucccggggcu gcgcgaggca 60

caggcg 66

<210> SEQ ID NO 327
<211> LENGTH: 119
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 327

agccugcgcc ggagccgggg ccugagcccg ggccgcgcag gccgugaacu cgucgagcug 60

cgcgugcggc cggugcucaa ccugccgggu ccuggccccg cgcucccgcg cgcccugga 119

<210> SEQ ID NO 328
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 328

ccucugugag aaagggugug ggggagaggc ugucuugugu cuguaaguau gccaaacuua 60

uuuuccccaa ggcagaggga 80

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<210> SEQ ID NO 329
<211> LENGTH: 74
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 329

gcagcccggu gagcgcucgc uggccuggca gugcgucgga agaacagggc gggugggccc 60

gcgcacaucu cugc 74

<210> SEQ ID NO 330
<211> LENGTH: 53
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 330

gguggggguu ggaggcgugg guuuuagaac cuaucccuuu cuagcccuga gca 53

<210> SEQ ID NO 331
<211> LENGTH: 93
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 331

guaaggaggg ggaugagggg ucauaucucu ucucagggaa agcaggagcc cuucagcagg 60

gucagggccc cucaucuucc ccuccuuucc cag 93

<210> SEQ ID NO 332
<211> LENGTH: 98
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 332

cuuggucaau aggaaagagg ugggaccucc uggcuuuucc ucugcagcau ggcucggacc 60

uagugcaaug uuuaagcucc ccucucuuuc cuguucag 98

<210> SEQ ID NO 333
<211> LENGTH: 92
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 333

gugagccagu ggaauggaga ggcugugggc agggggagau gugaaggaaa gaacuaggac 60

ccauucaucc acugcauucc ugcuuggccc ag 92

<210> SEQ ID NO 334
<211> LENGTH: 94
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 334

cacgugucc ccugguggaa ccuggcaggg ggagagguaa ggucuuucag ccucuccaaa 60

gcccaugguc agguacucag gugggggagc ccug 94

<210> SEQ ID NO 335
<211> LENGTH: 60
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 335

ugugaaugac ccccuuccag agccaaaauc accagggaug gaggaggggu cuuggguacu 60

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<210> SEQ ID NO 336
<211> LENGTH: 70
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 336

aaaagccugu cccuaagucc cucccagccu uccagaguug gugccaggaa ggauuuaggg 60

acaggcuuug 70

<210> SEQ ID NO 337
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 337

ucugggcgag gggugggcuc ucagaggggc uggcaguacu gcucugaggc cugccucucc 60

ccag 64

<210> SEQ ID NO 338
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 338

gucagagggg ggaugugcau gcugguuggg gugggcugcc uguggaccaa ucagcgugca 60

cuuccccacc cugaa 75

<210> SEQ ID NO 339
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 339

agggagaagg gucggggcag ggagggcagg gcaggcucug ggguggggggg ucugugaguc 60

agccacggcu cugcccacgu cucccc 86

<210> SEQ ID NO 340
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 340

gaaaacaacc aggugggcuu cccggagggc ggaacaccca gccccagcau ccagggcuca 60

ccuaccacgu uug 73

<210> SEQ ID NO 341
<211> LENGTH: 77
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 341

gaguugggag guucccucuc caaaauguguc uugaucccccc accccaagac acauuuggag 60

agggacccuc ccaacuc 77

<210> SEQ ID NO 342
<211> LENGTH: 61
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 342

ucacccggug agggcgggug gaggaggagg gucccacca ucagccuuca cugggacggg 60

a 61

<210> SEQ ID NO 343
<211> LENGTH: 119
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 343

ccaugaggag cuggcagugg gauggccugg ggguaggagc guggcuucug gagcuagacc 60

acauggguuc agaucccagc ggugccucua acuggccaca ggaccuuggg cagucagcu 119

<210> SEQ ID NO 344
<211> LENGTH: 70
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 344

gucccugggg gcugggaugg gccauggugu gcucugaucc cccugugguc ucuuggcccc 60

caggaacucc 70

<210> SEQ ID NO 345
<211> LENGTH: 74
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 345

gggaggaaga agggaggagg agcggagggg cccuugucuu cccagagccu cucccuuccu 60

ccccucccc uccc 74

<210> SEQ ID NO 346
<211> LENGTH: 66
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 346

acccaggagg cggaggaggu ggagguugca gugagccaag aucguggcac ugacuccagc 60

cugggg 66

<210> SEQ ID NO 347
<211> LENGTH: 102
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 347

gugggagggc ccaggcgcgg gcaggggugg ggguggcaga gcgcuguccc gggggcgggg 60

ccgaagcgcg gcgaccguaa cuccuucugc uccgucccc ag 102

<210> SEQ ID NO 348
<211> LENGTH: 113
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 348

gccggguggg gcggggcggc cucaggaggg gcccagcucc ccuggaugug cugcgguggg 60

gccggagggg cgucacgugc acccaaguga cgccccuucu gauucugccu cag 113

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<210> SEQ ID NO 349
<211> LENGTH: 91
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 349

acgccccccg ccccgccacc gccuuggagg cugaccucuu acuuucgguc ggucuucuuc 60

ccugggcuug guuuggggge gggggagugu c 91

<210> SEQ ID NO 350
<211> LENGTH: 54
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 350

agcagcaggg gagagagagg aguccucuag acaccgacuc ugucuccugc agau 54

<210> SEQ ID NO 351
<211> LENGTH: 136
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 351

ccgcuugccu cgcccagcgc agccccggcc gcugggcgca cccgucccgu ucgucccccgg 60

acguugcucu cuaccccggg aacgucgaga cuggagcgcc cgaacugagc caccuucgcg 120

gaccccgaga gcggcg 136

<210> SEQ ID NO 352
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 352

cugcagcgug cuucuccagg ccccgcgcgc ggacagacac acggacaagu cccgccaggg 60

gcugggcgcg cgccagccgg 80

<210> SEQ ID NO 353
<211> LENGTH: 47
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 353

cucggcgcgg ggcgcgggcu ccggguuggg gcgagccaac gccgggg 47

<210> SEQ ID NO 354
<211> LENGTH: 50
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 354

acccgggcgu ggugguggggg gugggugccu guaauuccag cuaguuggga 50

<210> SEQ ID NO 355
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 355

gugaggaggg gcuggcaggg accccuccaa guuggggacg gcagccagcc ccugcucacc 60

ccucgcc 67

<210> SEQ ID NO 356
<211> LENGTH: 106
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 356

agaagaaugc ccaaccagcc cucaguugcu acaguucccu guuguuucag cucgacaaca 60

acaggcggcu guagcaaugg ggggcuggau gggcaucuca augugc 106

<210> SEQ ID NO 357
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 357

ugugggcagg gcccuggga gcugaggcuc uggggguggc cggggcugac ccugggccuc 60

ugcuccccag ugucugaccg cg 82

<210> SEQ ID NO 358
<211> LENGTH: 69
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 358

cuuucggcca gcgggacggc auccgaggug ggcuaggcuc gggcccgugg cgggugcggg 60

ggugggagg 69

<210> SEQ ID NO 359
<211> LENGTH: 98
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 359

uugggcaagg ugcggggcua gggcuaacag cagucuuacu gaagguuucc uggaaaccac 60

gcacaugcug uugccacuaa ccucaaccuu acucgguc 98

<210> SEQ ID NO 360
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 360

accugaggag ccagcccucc ucccgcaccc aaacuuggag cacuugaccu uuggcuguug 60

gaggggcag gcucgcgggu 80

<210> SEQ ID NO 361
<211> LENGTH: 92
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 361

ccugucccuc cugcccugcg ccugcccagc ccuccugcuc uggugacuga ggaccgccag 60

gcaggggcug gugcugggcg gggggcggcg gg 92

<210> SEQ ID NO 362
<211> LENGTH: 79
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 362

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gugagguggg ggccagcagg gagugggcug ggcugggcug ggccaaggua caaggccuca 60

cccugcaucc cgcacccag 79

<210> SEQ ID NO 363
<211> LENGTH: 84
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 363

ccgcagccgc cgcgccgggc ccggguuggc cgcugacccc cgcggggccc ccggcggccg 60

gggcgggggc gggggcugcc ccgg 84

<210> SEQ ID NO 364
<211> LENGTH: 65
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 364

agcccugggg guggucucua gccaaggcuc uggggucuca cccuuggcug gucucugcuc 60

cgcag 65

<210> SEQ ID NO 365
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 365

gguuccggag ccccggcgcg ggcggguucu gggguguaga cgcugcuggc cagcccgccc 60

cagccgaggu ucucggcacc 80

<210> SEQ ID NO 366
<211> LENGTH: 97
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 366

aucugaguug ggaggguccc ucuccaaaug ugucuuggggg ugggggauca agacacauuu 60

ggagagggaa ccucccaacu cggccucugc caucauu 97

<210> SEQ ID NO 367
<211> LENGTH: 59
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 367

cuccagggag acagugugug aggccucuug ccauggccuc ccugcccgcc ucucugcag 59

<210> SEQ ID NO 368
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 368

gugggagggg agaggcagca agcacacagg gccugggacu agcaugcuga ccucccuccu 60

gccccag 67

<210> SEQ ID NO 369
<211> LENGTH: 115
<212> TYPE: RNA

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 369

gagcaaaaac cagagaacaa caugggagcg uuccuaaccc cuaaggcaac uggaugggag 60

accugaccca uccaguucuc ugagggggcu cuuguguguu cuacaagguu guuca 115

<210> SEQ ID NO 370
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 370

uuugguacuu gaagagagga uacccuuugu auguucacuu gauuaauggc gaauauacag 60

ggggagacuc uuauuugcgu aucaaa 86

<210> SEQ ID NO 371
<211> LENGTH: 70
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 371

ugugcacuug ggcaggaggg acccuguaug ucucccgca gcaccgucau cgugucccuc 60

uuguccacag 70

<210> SEQ ID NO 372
<211> LENGTH: 81
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 372

uacaggugca ggggaacugu agaugaaaag gcuuggcacu ugagggaaag ccucaguuca 60

uucucauuuu gcucaccugu u 81

<210> SEQ ID NO 373
<211> LENGTH: 63
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 373

gagucgagga cugguggaag ggccuuuccc cucagaccaa ggcccuggcc ccagcuucuu 60

cuc 63

<210> SEQ ID NO 374
<211> LENGTH: 103
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 374

gugucggcug uggcgugacu gucccucugu gucccccacu aggcccacug cucaguggag 60

cguggaggac gaggaggagg ccguccacga gcaaugccag cau 103

<210> SEQ ID NO 375
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 375

aauagauuau uggucaccac cuccaguuuc ugaauuugug agacuggggu ggggccugag 60

aauuugc 67

<210> SEQ ID NO 376
<211> LENGTH: 84
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 376

ugugcagugg gaaggggggc cgauacacug uacgagagug aguagcaggu cucacaguga 60

accggucucu uucccuacug uguc 84

<210> SEQ ID NO 377
<211> LENGTH: 70
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 377

aggacccagc ggggcugggc gcgcggagca gcgcugggug cagcgccugc gccggcagcu 60

gcaagggccg 70

<210> SEQ ID NO 378
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 378

ugcucuguag gcaugaggca gggcccaggu uccaugugau gcugaagcuc ugacauuccu 60

gcag 64

<210> SEQ ID NO 379
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 379

cugggggagg aaggacaggc caucugcuau ucguccacca accugacuug auccucucuu 60

cccuccuccc ag 72

<210> SEQ ID NO 380
<211> LENGTH: 69
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 380

ugggguaggg gugggggaau ucaggggugu cgaacucaug gcugccaccu uuguguccc 60

auccugcag 69

<210> SEQ ID NO 381
<211> LENGTH: 70
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 381

cucgggcccg accgcgccgg cccgcaccuc ccggcccgga gcugcgggcu gcggucaggg 60

cgaucccggg 70

<210> SEQ ID NO 382
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 382

cugacuuuuu uagggaguag aaggggugggg agcaugaaca auguuucuca cucccuaccc 60

cuccacuccc caaaaaaguc ag 82

<210> SEQ ID NO 383
<211> LENGTH: 79
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 383

gugcagaucc uugggagccc uguuagacuc uggauuuuac acuuggagug aacgggcgcc 60

aucccgaggc uuugcacag 79

<210> SEQ ID NO 384
<211> LENGTH: 71
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 384

auggaggggg guguggagcc agggggccca ggucuacagc uucuccccgc ucccugcccc 60

cauacuccca g 71

<210> SEQ ID NO 385
<211> LENGTH: 92
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 385

cgcugcgcuu cugggcccgc ggcgggcgug gggcugcccg ggccggucga ccagcgcgcc 60

guagcucccg aggcccgagc cgcgacccgc gg 92

<210> SEQ ID NO 386
<211> LENGTH: 97
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 386

cucaggugcu cuggcugcuu ggguuccugg caugcugauu ugugacuuaa gauuaaaauc 60

acauugccag ggauuaccac gcaaccacga ccuuggc 97

<210> SEQ ID NO 387
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 387

ggccggcugg gguuccuggg gaugggauuu gcuuccuguc acaaaucaca uugccaggga 60

uuuccaaccg acc 73

<210> SEQ ID NO 388
<211> LENGTH: 85
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 388

aggguagagg gaugaggggg aaaguucuau aguccuguaa uuagaucuca ggacuauaga 60

acuuuccccc ucaucccucu gcccu 85

<210> SEQ ID NO 389
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 389

ucuaagaaac gcaguggucu cugaagccug caggggcagg ccagcccugc acugaacgcc 60

uguucuugcc agguggcaga agguugcugc 90

<210> SEQ ID NO 390
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 390

accucuaccu cccggcagag gaggcugcag aggcuggcuu uccaaaacuc ugcccccucc 60

gcugcugcca aguggcuggu 80

<210> SEQ ID NO 391
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 391

ucaucccugg gugggguuu guugcauuac uuguguucua uauaaaguau ugcacuuguc 60

ccggccugug gaaga 75

<210> SEQ ID NO 392
<211> LENGTH: 109
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 392

ggucgggcuc accaugacac agugugagac cucgggcuac aacacaggac ccgggcgcug 60

cucugacccc ucgugucuug uguugcagcc ggagggacgc agguccgca 109

<210> SEQ ID NO 393
<211> LENGTH: 89
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 393

gucagcagug ccuuagcagc acguaaauau uggcguuaag auucuaaaau uaucuccagu 60

auuaacugug cugcugaagu aagguugac 89

<210> SEQ ID NO 394
<211> LENGTH: 81
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 394

guuccacucu agcagcacgu aaauauuggc guagugaaau auauauuaaa caccaauauu 60

acugugcugc uuuaguguga c 81

<210> SEQ ID NO 395
<211> LENGTH: 96
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 395

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cgggccccgg gcgggcggga gggacgggac gcggugcagu guuguuuuuu cccccgccaa 60

uauugcacuc gucccggccu ccggcccccc cggccc 96

<210> SEQ ID NO 396
<211> LENGTH: 84
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 396

cuccccaugg cccugucucc caacccuugu accagugcug ggcucagacc cugguacagg 60

ccugggggac agggaccugg ggac 84

<210> SEQ ID NO 397
<211> LENGTH: 94
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 397

cgggcagcgg gugccaggca cggugucagc aggcaacaug gccgagaggc cggggccucc 60

gggcggcgcc guguccgcga ccgcguaccc ugac 94

<210> SEQ ID NO 398
<211> LENGTH: 86
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 398

ugccagucuc uaggucccug agacccuuua accugugagg acauccaggg ucacagguga 60

gguucuuggg agccuggcgu cuggcc 86

<210> SEQ ID NO 399
<211> LENGTH: 78
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 399

cuuucuacac agguugggau cgguugcaau gcuguguuuc uguaugguau ugcacuuguc 60

ccggccuguu gaguuugg 78

<210> SEQ ID NO 400
<211> LENGTH: 93
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 400

ccuuccggcg ucccaggcgg ggcgccgcgg gaccgcccuc gugucugugg cggugggauc 60

ccgcggccgu guuuuccugg uggcccggcc aug 93

<210> SEQ ID NO 401
<211> LENGTH: 83
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 401

gucuacuccc agggugccaa gcuguuucgu guucccuccc uaggggaucc cagguagggg 60

cagcagagga ccugggccug gac 83

<210> SEQ ID NO 402
<211> LENGTH: 72

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<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 402

ugugggacug caaaugggag cucagcaccu gccugccacc cacgcagacc agccccugcu 60

cuguucccac ag 72

<210> SEQ ID NO 403
<211> LENGTH: 110
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 403

gucuaccagg ugugggccca gcuuuacaua guucaugcug aggccgggau uucaugcaga 60

aaacugguug caaaaggugc ugaaggggcu gggggagcac aagggagaag 110

<210> SEQ ID NO 404
<211> LENGTH: 89
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 404

agccugugg aaagagaaga gcagggcagg gugaaggccc ggcggagaca cucugcccac 60

cccacacccu gccuaugggc cacacagcu 89

<210> SEQ ID NO 405
<211> LENGTH: 62
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 405

gaggguggug gaggaagagg gcagcuccca ugacugccug accgccuucu cuccuccccc 60

ag 62

<210> SEQ ID NO 406
<211> LENGTH: 75
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 406

uggaguggg gggcaggagg ggcucaggga gaaagugcau acagccccug gcccucucug 60

cccuuccguc cccug 75

<210> SEQ ID NO 407
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 407

ccaggcacac aggaaaagcg gggcccuggg uucggcugcu accccaaagg ccacauucuc 60

cugugcacac ag 72

<210> SEQ ID NO 408
<211> LENGTH: 153
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 408

gcuccgcccc acgucgcaug cgccccggga acgcgugggg cggagcuucc ggaggccccg 60

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cucugcugcc gacccugugg agcggagggu gaagccuccg gaugccaguc ccucaucgcu 120

ggccuggucg cgcuguggcg aaggggggcgg agc 153

<210> SEQ ID NO 409
<211> LENGTH: 153
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 409

gcuccgcccc acgucgcaug cgccccggga acgcgugggg cggagcuucc ggaggccccg 60

cccugcugcc gacccugugg agcggagggu gaagccuccg gaugccaguc ccucaucgcu 120

ggcccggucg cgcuguggcg aaggggggcgg agc 153

<210> SEQ ID NO 410
<211> LENGTH: 49
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 410

ggugaggcgg gggggcgagc ccugaggggc ucucgcuucu ggcgccaag 49

<210> SEQ ID NO 411
<211> LENGTH: 100
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 411

gaggugggag gauugcuuga gucagggugg uugaggcugc aguaaguugu gaucauacca 60

cugcacucca gccugaguga cagagcaaga ccuugucuca 100

<210> SEQ ID NO 412
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 412

ggguggggggc ggggcggcag gggccucccc cagugccagg ccccauucug cuucucuccc 60

agcu 64

<210> SEQ ID NO 413
<211> LENGTH: 74
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 413

ccugcaggag gcaguggggcg agcaggcggg gcagcccaau gccaugggcc ugaucucacc 60

gcugccuccu uccc 74

<210> SEQ ID NO 414
<211> LENGTH: 60
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 414

aggccuaggg gguggcaggc uggccaucag uguggggcuaa cccuguccuc ucccucccag 60

<210> SEQ ID NO 415
<211> LENGTH: 100
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 415

gugagcgggc gcggcaggga ucgcgggcgg guggcggccu agggcgcgga gggcggaccg 60

ggaauggcgc gccgugcgcc gccggcguaa cugcggcgcu 100

<210> SEQ ID NO 416
<211> LENGTH: 56
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 416

guaggcaggg gcugggguuu cagguucuca gucagaaccu uggccccucu ccccag 56

<210> SEQ ID NO 417
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 417

ucuccucgag gggucucugc cucuacccag gacucuuuca ugaccaggag gcugaggccc 60

cucacaggcg gc 72

<210> SEQ ID NO 418
<211> LENGTH: 68
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 418

gcauccugua cugagcugcc ccgaggcccu ucaugcugcc cagcucgggg cagcucagua 60

caggauac 68

<210> SEQ ID NO 419
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 419

uccuguacug agcugccccg agcugggcag caugaagggc cucggggcag cucaguacag 60

gaug 64

<210> SEQ ID NO 420
<211> LENGTH: 54
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 420

acgcgggugc gggccggcgg gguagaagcc acccggcccg gcccggcccg gcga 54

<210> SEQ ID NO 421
<211> LENGTH: 89
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 421

accaugcugu agugugugua aacauccuac acucucagcu gugagcucaa gguggcuggg 60

agaggguugu uuacuccuuc ugccaugga 89

<210> SEQ ID NO 422
<211> LENGTH: 85
<212> TYPE: RNA

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 422

gugagcugcu ggggacgcgg gucggggucu gcagggcggu gcggcagccg ccaccugacg 60

ccgcgccuuu gucugugucc cacag 85

<210> SEQ ID NO 423
<211> LENGTH: 71
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 423

ggguaaaggg gcagggacgg guggccccag gaagaagggc cugguggagc cgcucuucuc 60

ccugcccaca g 71

<210> SEQ ID NO 424
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 424

ggggagguac cugggacagg aggaggaggc agccuugccu cagaaaccaa acugucaaaa 60

guguagguuc cac 73

<210> SEQ ID NO 425
<211> LENGTH: 90
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 425

cgggcggggc ggguccggcc gccuccgagc ccggccggca gcccccggcc uuaaagcgcg 60

ggcuguccgg aggggucggc uuucccaccg 90

<210> SEQ ID NO 426
<211> LENGTH: 83
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 426

acggcaucuu ugcacucagc aggcaggcug gugcagcccg ugguggggga ccauccugcc 60

ugcugugggg uaaggacggc ugu 83

<210> SEQ ID NO 427
<211> LENGTH: 63
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 427

gagguguagg ggagguuggg ccagggaugc cuucacugug ucucucuggu cuugccaccc 60

cag 63

<210> SEQ ID NO 428
<211> LENGTH: 72
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 428

cugugcaccu gggggagugc agugauugug gaaugcaaag ucccacaauc acuguacucc 60

ccaggugcac ag 72

<210> SEQ ID NO 429
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 429

guggcacuca aacugugggg gcacuuucug cucucuggug aaagugccgc caucuuuuga 60

guguuac 67

<210> SEQ ID NO 430
<211> LENGTH: 62
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 430

gguaggggge gggcuccggc gcugggaccc cacuagggug gcgccuuggc cccgccccgc 60

cc 62

<210> SEQ ID NO 431
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 431

gugaguggga ggccagggca cggcaggggg agcugcaggg cuaugggagg ggccccagcg 60

ucugagcccu guccuccegc ag 82

<210> SEQ ID NO 432
<211> LENGTH: 82
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 432

gugaguggga ggccagggca cggcaggggg agcugcaggg cuaugggagg ggccccagcg 60

ucugagcccu guccuccegc ag 82

<210> SEQ ID NO 433
<211> LENGTH: 81
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 433

aguugguggg ggagccauga gauaagagca ccuccuagag aauguugaac uaaaggugcc 60

cucucuggcu ccucccccaaa g 81

<210> SEQ ID NO 434
<211> LENGTH: 68
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 434

cuccggugcc uacugagcug auaucaguuc ucauuuuaca cacuggcuca guucagcagg 60

aacaggag 68

<210> SEQ ID NO 435
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 435

cucugccucc cgugccuacu gagcugaaac acaguugguu uguguacacu ggcucaguuc 60

agcaggaaca ggg 73

<210> SEQ ID NO 436
<211> LENGTH: 83
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 436

gugaguggga gccccagugu gugguugggg ccauggcggg ugggcagccc agccucugag 60

ccuuccucgu cugucugccc cag 83

<210> SEQ ID NO 437
<211> LENGTH: 67
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 437

gcgcccuccc ucucuccccg gugugcaaau gugugugugc gguguuaugc cggacaagag 60

ggaggug 67

<210> SEQ ID NO 438
<211> LENGTH: 58
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 438

gcugaagcuc uaagguuccg ccugcgggca ggaagcggag gaaccuugga gcuucggc 58

<210> SEQ ID NO 439
<211> LENGTH: 80
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 439

gagaggccaa gaccuuggga auggggguaa gggccuucug agcccagguc cgaacucucc 60

auuccucugc agagcgcucu 80

<210> SEQ ID NO 440
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 440

ccccgggccc ggcguucccu ccccuuccgu gcgccagugg aggccggggu ggggcggggc 60

gggg 64

<210> SEQ ID NO 441
<211> LENGTH: 64
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 441

ccccgggccc ggcguucccu ccccuuccgu gcgccagugg aggccggggu ggggcggggc 60

gggg 64

<210> SEQ ID NO 442
<211> LENGTH: 85

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<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 442

ggggagguag ggaaaaggaa gggggaggag aaggugagac caauguccug ggugccacuc 60

cugcccagug ccucccuucc ucguu 85

<210> SEQ ID NO 443
<211> LENGTH: 73
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 443

guucaagugg gaggacagga ggcaggugug guuggaggaa gcagccugaa ccugccuccc 60

ugacauucca cag 73

<210> SEQ ID NO 444
<211> LENGTH: 98
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 444

agaaugggca aaugaacagu aaauuuggag gccuggggcc cucccugcug cuggagaagu 60

guuugcacgg gugggccuug ucuuugaaag gaggugga 98

<210> SEQ ID NO 445
<211> LENGTH: 60
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 445

cgcugggucc gcgcgcccug ggccgggcga uguccgcuug ggggagcgag gggcggggcg 60

<210> SEQ ID NO 446
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 446

cuccuggggc ccgcacucuc gcu 23

<210> SEQ ID NO 447
<211> LENGTH: 18
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 447

cuccuggggc ccgcacuc 18

<210> SEQ ID NO 448
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 448

caacucugau cucuucaucu a 21

<210> SEQ ID NO 449
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 449

ucucuucauc uacccccag 20

<210> SEQ ID NO 450
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 450

ggugggugag gucgggcccc aag 23

<210> SEQ ID NO 451
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 451

cgggguggggu gaggucgggc 20

<210> SEQ ID NO 452
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 452

ccuucuggag aggcuuugug cggaua 26

<210> SEQ ID NO 453
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 453

ccuucuggag aggcu 15

<210> SEQ ID NO 454
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 454

ggcuggucag augggagugg 20

<210> SEQ ID NO 455
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 455

ggcuggucag augggagugg 20

<210> SEQ ID NO 456
<211> LENGTH: 26
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 456

aggagggagg agaugggcca aguucc 26

<210> SEQ ID NO 457
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 457

gggaggaggg aggag 15

<210> SEQ ID NO 458
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 458

cuucccccca guaaucuuca u 21

<210> SEQ ID NO 459
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 459

cuucccccca guaaucuuca u 21

<210> SEQ ID NO 460
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 460

cggauccgag ucacggcacc a 21

<210> SEQ ID NO 461
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 461

ggauccgagu cacgg 15

<210> SEQ ID NO 462
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 462

cccaggcugg agcgagugca g 21

<210> SEQ ID NO 463
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 463

agcucacugc agccu 15

<210> SEQ ID NO 464
<211> LENGTH: 17
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 464

uccuagucac ggcacca 17

<210> SEQ ID NO 465
<211> LENGTH: 17
<212> TYPE: RNA

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<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 465

uccuagucac ggcacca 17

<210> SEQ ID NO 466
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 466

gaggcuggga aggcaaaggg acgu 24

<210> SEQ ID NO 467
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 467

gaaggaggcu gggaa 15

<210> SEQ ID NO 468
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 468

gaggcgaugu ggggauguag a 21

<210> SEQ ID NO 469
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 469

cccagucuca uuuccucauc 20

<210> SEQ ID NO 470
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 470

ggcccggccg ugccugaggu uuc 23

<210> SEQ ID NO 471
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 471

ggcgguggga ucccg 15

<210> SEQ ID NO 472
<211> LENGTH: 16
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 472

cuggggucc cccgac 16

<210> SEQ ID NO 473
<211> LENGTH: 15

<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 473

guguggagcu ggggc 15

<210> SEQ ID NO 474
<211> LENGTH: 25
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 474

agcggggagg aagugggcgc ugcuu 25

<210> SEQ ID NO 475
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 475

agcggggagg aagugggcgc u 21

<210> SEQ ID NO 476
<211> LENGTH: 27
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 476

aaaccguuac cauuacugag uuuagua 27

<210> SEQ ID NO 477
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 477

gaaaccguua ccauu 15

<210> SEQ ID NO 478
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 478

caggcacggg agcucaggug ag 22

<210> SEQ ID NO 479
<211> LENGTH: 17
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 479

caggcacggg agcucag 17

<210> SEQ ID NO 480
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 480

gggggucccc ggugcucgga ucu 23

<210> SEQ ID NO 481

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<211> LENGTH: 16
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 481

ucgggagggg cgggag 16

<210> SEQ ID NO 482
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 482

cggggccgua gcacugucug aga 23

<210> SEQ ID NO 483
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 483

cggggccgua gcacugucug 20

<210> SEQ ID NO 484
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 484

aucccaccac ugccaccauu 20

<210> SEQ ID NO 485
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 485

aucccaccac ugcca 15

<210> SEQ ID NO 486
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 486

acaggagugg gggugggaca uaa 23

<210> SEQ ID NO 487
<211> LENGTH: 20
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 487

acaggagugg gggugggaca 20

<210> SEQ ID NO 488
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 488

cuggggacg cgugagcgcg agc 23

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<210> SEQ ID NO 489
<211> LENGTH: 21
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 489

cuggggacg cgugagcgcg a 21

<210> SEQ ID NO 490
<211> LENGTH: 22
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 490

cgcggcgggg acggcgauug gu 22

<210> SEQ ID NO 491
<211> LENGTH: 17
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 491

cggcggggac ggcgauu 17

<210> SEQ ID NO 492
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 492

gagggccccc ccucaauccu guu 23

<210> SEQ ID NO 493
<211> LENGTH: 16
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 493

agggcccccc cucaau 16

<210> SEQ ID NO 494
<211> LENGTH: 30
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 494

ugaggggcag agagcgagac uuuucuauuu 30

<210> SEQ ID NO 495
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 495

ugaggggcag agagc 15

<210> SEQ ID NO 496
<211> LENGTH: 24
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 496

gugaguggga gccggugggg cugg 24

<210> SEQ ID NO 497
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 497

ggggcuggag uaagg 15

<210> SEQ ID NO 498
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 498

ugaggauaug gcagggaagg gga 23

<210> SEQ ID NO 499
<211> LENGTH: 19
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 499

ugaggauaug gcagggaag 19

<210> SEQ ID NO 500
<211> LENGTH: 23
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 500

cuaguggaag aagauggcgg aag 23

<210> SEQ ID NO 501
<211> LENGTH: 15
<212> TYPE: RNA
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 501

uaguggaaga agaug 15

<210> SEQ ID NO 502
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gugggggggc aggagg 16

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ggcgcggagg gcggac 16

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aggaggagga ggcag 15

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gugugcggug uuaug 15

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uaucccccag 69

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ggcuccuugg ucuaggggua augcca 86

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guuuuccucc gguucucagg gcuccaccuc uuucgggccg uagagccagg gcuggugc 118

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aggcagggcc cccgcucccc gggccugacc ccac 94

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ugcucacugc cccgucccgg cgcccguguc uccuccag 98

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ggaaaaaggc gggagaagcc cca 83

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<400> SEQUENCE: 738

ggacaagggc ggcgcgaccg gcccggggcu cuugggcggc cgcguuuccc cucc 54

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cuccacaggc cuggug 76

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cucag 65

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ccuguag 67

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<400> SEQUENCE: 747

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<400> SEQUENCE: 748

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<210> SEQ ID NO 749
<211> LENGTH: 15
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<400> SEQUENCE: 749

aggaagagga ggaag 15

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<400> SEQUENCE: 750

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<210> SEQ ID NO 751
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<400> SEQUENCE: 751

gcugggcggg gcgcg 15

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<400> SEQUENCE: 752

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<210> SEQ ID NO 753
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<400> SEQUENCE: 753

uggggaaggc gucagu 16

<210> SEQ ID NO 754
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<400> SEQUENCE: 754

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<400> SEQUENCE: 755

gggcccccgc ucccc 15

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<400> SEQUENCE: 761

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<213> ORGANISM: Homo sapiens

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<210> SEQ ID NO 764
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cccgguguug gggcgcgucu g 21

The invention claimed is:

1. A method for detecting liver cancer, comprising determining an expression level of hsa-miR-1343-3p in a sample of a subject using a kit comprising a nucleic acid(s), as a primer(s) for PCR, or as a probe(s) for Northern blotting, Southern blotting, or in situ hybridization, capable of specifically binding to hsa-miR-1343-3p, wherein the determining comprises the following steps of:

(a) contacting hsa-miR-1343-3p in the sample or complementary polynucleotide(s) thereof prepared from hsa-miR-1343-3p with the nucleic acid(s);

(b) measuring an expression level of hsa-miR-1343-3p by quantitative RT-PCR using the nucleic acid(s) as the primer(s), or Northern blotting, Southern blotting, or in situ hybridization using the nucleic acids as the probe(s); and

(c) comparing the expression level of hsa-miR-1343-3p measured in step (b) with a control expression level of hsa-miR-1343-3p in a control sample of a healthy subject measured in the same way as in step (b), wherein a lower expression level of hsa-miR-1343-3p in the sample of the subject as compared to the control expression level is detected and is indicative that the subject has liver cancer; and

treating the subject for liver cancer or performing a diagnostic procedure on the liver of the subject, wherein the treatment comprises: surgical resection and/or liver transplantation; local therapy which involves injecting a drug through centesis or performing cauterization to kill cancer; or hepatic arterial embolization; optionally in combination with a drug therapy or radiotherapy, and wherein the diagnostic procedure comprises a palpation or imaging test,

wherein the subject is human, and wherein the sample is blood, serum, or plasma.

2. A method for detecting liver cancer, comprising determining an expression level of hsa-miR-1343-3p in a sample of a subject using a device comprising a nucleic acid(s), as a probe(s), capable of specifically binding to hsa-miR-1343-3p, wherein the determining comprises the following steps of:

(a) binding hsa-miR-1343-3p in the sample or cDNA thereof prepared from hsa-miR-1343-3p to the nucleic acid(s) to measure an expression level of hsa-miR-1343-3p by hybridization using the nucleic acid(s); and

(b) comparing the expression level of hsa-miR-1343-3p measured in step (a) with a control expression level of hsa-miR-1343-3p in a control sample of a healthy subject measured in the same way as in step (a), wherein a lower expression level of hsa-miR-1343-3p in the sample of the subject as compared to the control expression level is detected and is indicative that the subject has liver cancer; and

treating the subject for liver cancer or performing a diagnostic procedure on the liver of the subject, wherein the treatment comprises: surgical resection and/or liver transplantation; local therapy which involves injecting a drug through centesis or performing cauterization to kill cancer; or hepatic arterial embolization; optionally in combination with a drug therapy or radiotherapy, and wherein the diagnostic procedure comprises a palpation or imaging test,

wherein the subject is human, and wherein the sample is blood, serum, or plasma.

3. The method according to claim 1, wherein step (c) further comprises preparing a discriminant based on a formula.

4. The method according to claim 3, wherein the discriminant is compared to a threshold.

5. The method according to claim 2, wherein step (b) further comprises preparing a discriminant based on a formula.

6. The method according to claim 5, wherein the discriminant is compared to a threshold.

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